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TABLE *of* CONTENTS

SPECIAL ARTICLES

Technics and Potentialities of Intracranial Electrography
HENRY W. DODGE, JR., M.D., REGINALD G. BICKFORD, M.B., ALLAN A. BAILEY, M.D., COLIN B. HOLMAN, M.D., MAGNUS C. PETERSEN, M.D. AND CARL W. SEM-JACOBSEN, M.D. 291

Backache: Diagnosis and Treatment from an Orthopedic Standpoint
CARLO SCUDERI, M.D. 301

ACTH, Cortisone and Hydrocortisone; Rationale of Therapy
CAPT. CHRISTOPHER C. SHAW, MC, USN 308

Primary Closure of Open Injuries of the Hand
MICHAEL L. MASON, M.D. 315

DIAGNOSTIC CLINICS

Pancreatitis
ROBERT M. ZOLLINGER, M.D. 323

Mucoviscidosis: Its Clinical Aspects and Treatment
EARL H. BAXTER, M.D. 334

Asthma and Asthmatoid Dyspnea
THEODORE L. SQUIER, M.D. 342

Rehabilitation of the Hemiplegic
HOWARD A. RUSK, M.D. 347

SCIENTIFIC EXHIBIT

Emergency Examinations of the Newborn
GEORGE COOPER, JR., M.D. 353

PEDIATRICS IN GENERAL PRACTICE

Nephrosis in Children
HENRY L. BARNETT, M.D. AND MADOKA SHIBUYA, M.D. 362

(Continued on page A-6)

GENERAL PRACTICE REVIEW

Depressive Illness
HERVEY M. CLECKLEY, M.D. 370

Physical Diagnosis in Modern Medicine
FRIEDRICH W. NIEHAUS, M.D. 374

DEPARTMENTS

EDITORIALS 379

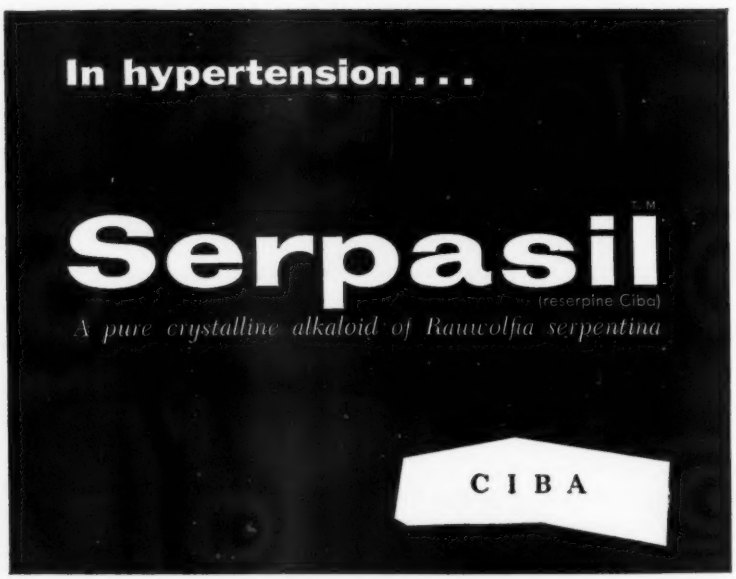
Operative Dictation

Death from Dicumarol Poisoning

Population Changes

POSTGRADUATE CLINICAL NOTES

16. The Face in Diagnosis. I. 314
17. The Face in Diagnosis. II. 322
18. The Face in Diagnosis. III. 352



Technics and Potentialities of Intracranial Electrography

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Intracranial electrography is an extension of scalp and surface electro-encephalography in which electric impulses are obtained from the depths of the human brain. The surgical technic required for the placement of deep electrodes is simple, and the multicontact electrodes are well tolerated. Pertinent information may be obtained by means of electric recording from or stimulation of the subcortex. This method portends to become a valuable diagnostic and investigative aid.

In an attempt to achieve better understanding of disorders of the central nervous system and to improve their medical and surgical treatment, investigation of cerebral electric potentials has been extended recently to include those arising from the subcortical depths. The recording of these depth potentials has been termed "depth electrography."

HENRY W. DODGE, JR.

Recording of impulses from the depth of the human brain is a combined procedure that necessitates the close cooperation of a team of physicians, as do modern procedures in many other fields of medicine. This report is concerned with the developmental background of this newer extension of electroencephalography, the surgical technics involved and the potential the future may hold as the result of further efforts in this field.

The term "depth electrography" which will be employed means the recording of brain-wave potentials and patterns from tiny electrodes inserted deeply into the substance of the human brain. When reference to recording from the scalp or cerebral surface is made, it will be differentiated from subcortical electric recording.

History and Development

Following the pioneer work of Berger, published in 1929, and the subsequent elaboration and extension of these technics by Adrian,

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Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

FIGURE 1 *(above)*. Relative size of an intracranial depth electrode and an ordinary brain cannula employed in routine neurosurgical diagnostic procedures.

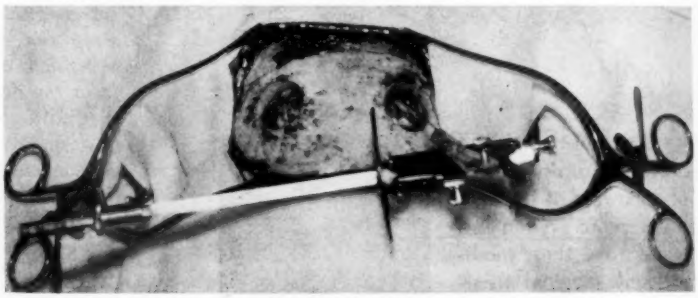

FIGURE 2 *(right)*. Stereotaxic localizer in place for introduction of depth electrodes into the frontal lobes. Note trephine openings through which bilateral prefrontal lobotomy will be done later.

scalp electro-encephalography rapidly became a useful and important aid in the diagnosis of disorders of the nervous system.

Although great advances were made in the recording and analysis of activity from the surface of the brain, it soon became evident that the cortical rhythms were only a component of the total activity. Hess'[1] application of methods of depth study in unanesthetized animals paved the way for many valuable contributions dealing with the electric activity of subcortical and deeper centers in animals.

Recording of human brain-wave patterns from the surface of the cortex was refined and brilliantly extended by Penfield and his coworkers and students in their studies of persons afflicted with epilepsy.[2] Sporadic studies had been made and reported by various investigators who utilized the deep exploring electrode at operation to investigate the rhythms encountered in the depths of the human brain.[3-6] However, the difficulty of obtaining consistently satisfactory recordings and valid reproducible results in the operating room led many observers to lose their initial enthusiasm. In an attempt to overcome some of the pitfalls of recording in the operating room, one of us (Bickford) and Cairns,[7] in 1944, inserted leads deep into wounds of the brains of soldiers injured by penetration of high-velocity missiles.

From this beginning has evolved the idea of interval depth recording, namely the recording of brain-wave patterns from the depths of the brain at a time remote from operation at the convenience of both the patient and the electro-encephalographer. Development has been slow and the hurdles numerous, but the intriguing possibilities offered by such study have maintained interest.

Briefly, some of the obstacles in human patients were concerned with the development of an adequate surgical technic, the prevention of infection and various problems concerned with the electrodes, including their stereotaxic localization,[8] their maintenance at the proper site, and their physical electric properties. In addition, considerable research was necessary to determine the tolerance of nervous and other tissue to the prolonged presence of such a foreign body as a metallic electrode. The electric equipment, recording devices and methods, and the significance of the results were all coincidental problems. Most important, of course, was the welfare of the patient; some of the lag in the rapid growth and expansion of this field was due

to the necessity that members of the investigating team convince themselves that valuable information could be gained by this method to the patient's benefit without needlessly endangering or harming him.

Similar projects are presently being carried on at several large centers.[9,10] The possibility of vastly increasing knowledge of cerebral function and at the same time bettering therapeutic methods led a team of physicians from the Rochester State Hospital, Rochester, Minnesota, and the Mayo Clinic some time ago to undertake intensive study of intracranial depth electrography in humans.

Technic

Two main groups of patients were chosen for beginning study in depth electrographic evaluation, namely, intractable epileptics and persons suffering from schizophrenia. Considered for study were only those patients in whom it appeared that operative intervention, either excision of epileptogenic foci or bilateral prefrontal lobotomy, was the ultimate necessary method of treatment. No patient was studied by depth methods who did not have an operation or in whom an operation was not intended. Prior to the insertion of depth electrodes, all patients received careful general and neurologic examinations, routine laboratory studies, roentgenologic surveys and such neurologic and neurosurgical tests as were individually indicated.

The surgical technic itself is simple[11] but has been possible only by the advent of adequate antibiotic drugs as prophylaxis against infection. Local anesthesia is induced after the scalp is shaved and surgically draped. The tiny multiwire electrodes (figure 1) may be placed through trephine openings later intended for prefrontal lobotomy, or through small perforator openings in the skull preliminary to other intracranial procedures. Stereotaxic localization is employed for placement, as shown in figure 2. The electrodes are tied into the cranial dura mater with silk sutures and allowed to exit from the operative wound, being identified by colored silk markers for later connection to miniature sockets (figures 3 and 4).

These multicontact electrodes consist of 40-gauge insulated copper wire bound into leads comprising six wires each, leading to six recording tips located at intervals of 1 cm. along each depth lead. The electrodes are completely insulated except for a 1 mm. area at each recording tip. Recently, it has appeared worth while to shift from copper to stainless steel electrodes. Usually six electrodes incorporating six contacts each, a total of 36 recording contacts, are employed, but any number of electrodes may be inserted depending on the

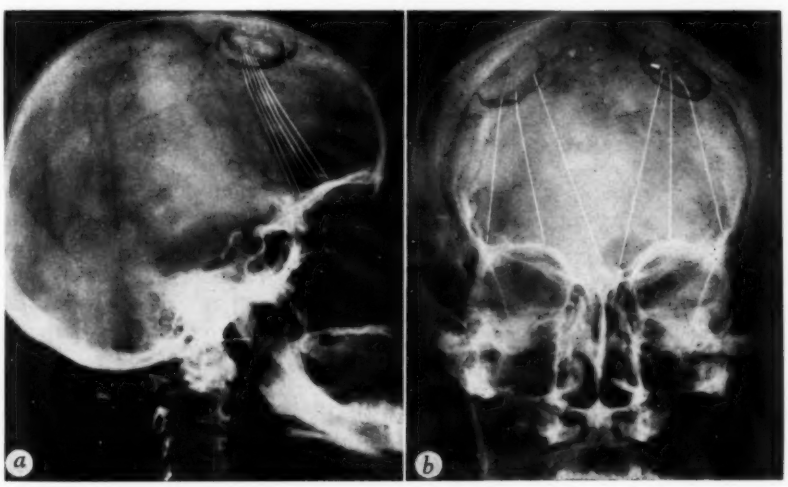

FIGURE 3. Postwiring roentgenograms prior to prefrontal lobotomy. a *(left)*. Wire shadows. b *(right)*. Intensified.

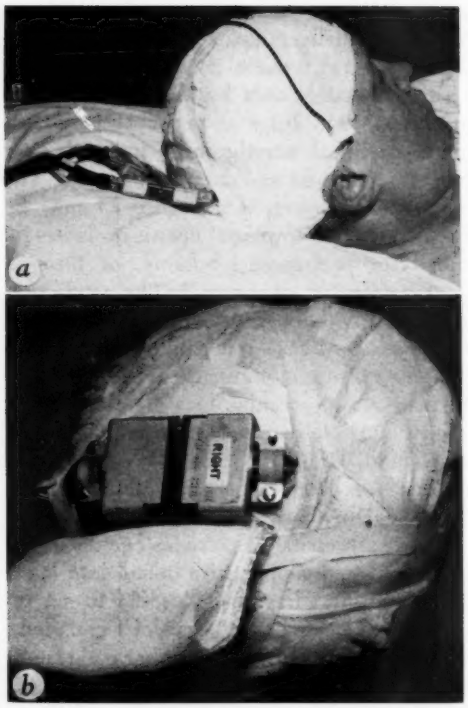

FIGURE 4a *(top)*. Miniature sockets attached to depth leads, allowing simple and rapid connection and disconnection of patient to recording machine. b *(bottom)*. Close-up view of same patient.

particular problem and the recording equipment available. We are presently utilizing a 16-channel Grass electro-encephalographic ink-recording machine with a special Gilson input switch capable of switching 20 channels to any of 60 contacts.

Careful consideration of the technic in an experience involving more than 40 patients, during which time every major area of the brain has been subjected to depth study, has led us to conclude that this procedure is safe and is not accompanied by undue risk.

Electrodes have been allowed to remain in place for periods up to six weeks. The apparent clinical innocuity of the procedure has been impressive. However, in the severely disturbed patient, in whom care of the wound is a problem, infection must be contended with on occasions. We have had one death from a brain abscess in such a patient. This is not a problem in nonpsychotic persons.

The patient who undergoes insertion of depth electrodes under local anesthesia often may go directly to the recording room. In the days following, he may walk or be taken in a wheel chair for daily recording sessions for varying periods, during which he may sit or lie at ease.

Patients have volunteered the information that the electrodes cause no discomfort. They may be connected and disconnected more rapidly and with less discomfort than when surface electrodes are used on the scalp. At the time when recording is done, the patient is unanesthetized, unmedicated and, except for the head dressing, unchanged from his usual everyday prewiring status (figure 5a). During recording remote from the operation, the electrographer may observe, photograph or talk to the patient. Various drugs, stimulants or depressants, may be employed to observe their effect on the brain-wave pattern. The frequency components of the electric recordings from different levels of the brain may be measured by use of the frequency analyzer. A high-frequency channel with audio-amplifier and speaker may be incorporated to parallel the main ink-writing channels. Photographs of discharges with a camera, listening to discharges over the loudspeaker and tape recording of sound discharges from the depths are all part of the technic and are easily permitted by interval depth recording. Studies in stimulation of the depths similarly may be undertaken by means of the depth electrodes; the response of the patient may be studied thoroughly and recorded by these multiple methods (figure 5b).

Apart from the information they give concerning activity within the substance of the brain, depth electrograms are almost free of artifacts caused by ocular movements, muscle action potentials and movements of the head. Pulse artifact rarely has been encountered, and an extremely satisfactory feature of the recordings from deep electrodes is their repeatability and reliability from day to day.

To those experienced in recording in the operating room, where the quantity of equipment, the necessity for aseptic technic, the temperaments of the surgeon, anesthetist and

electro-encephalographer, and the fear, apprehension and, finally, fatigue of the patient all combine to complicate the procedure, interval recording seems to offer much.

Potentialities

Discussion of the future potentialities of depth electrography is best considered in the light of some of the more interesting findings to date. It appears highly unlikely that depth electrography will ultimately replace the technic of recording from the scalp and surface of the brain. However, with this latest addition, the electrographer has at his command a tool the possibilities of which appear promising.

A comparison of brain-wave tracings from the subcortex and depths with tracings obtained from the scalp has been likened to the difference between looking through a bright clean glass window and trying to peer out of a frosted glass pane. As mentioned previously, pleasing dividends from use of depth leads are the lack of artifacts and the reliable repeatability of the tracings.

Analysis of depth electrograms gives the impression that the normal rhythms so familiar in records from the scalp and cerebral surface extend widely diffused into the depths of the brain and show little tendency to sharp localization. This is somewhat surprising, for rather sharp topographic functional localization is known to exist in the human brain. Some strength is added by the above finding to the suggestion that the so-called normal

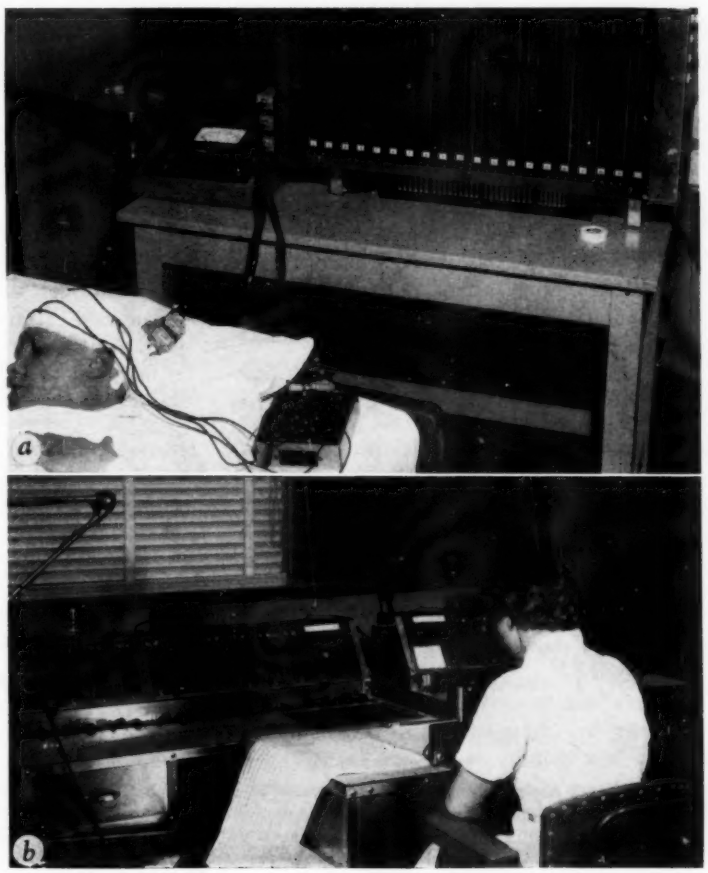

FIGURE 5a *(top)*. Patient lying at ease and unmedicated and unanesthetized during a recording session. Note the special Gilson input switch in right background. b *(bottom)*. Grass 16-channel electro-encephalographic machine used for permanent ink tracings of depth potentials.

spontaneous rhythms of the human brain are not direct results of local functional activity.

On the basis of these observations, one immediately wonders if electric mapping of the subcortex and cerebral depths can be achieved so that the particular zone being studied can be recognized by the record of its electric activity. If such recognizable subcortical mapping could be achieved, a newer and more physiologic approach to many obscure neurologic disorders could be anticipated.

The availability of the patient to whom depth electrodes have been attached has allowed considerable extension of previously reported work concerning the clinical testing of various drugs and the effect of anesthesia. Recordings from the depths with the patient under deep anesthesia induced by thiopental sodium (PENTOTHAL® sodium) have suggested the presence of a diffuse synchronizing cerebral network in humans such as had been demonstrated previously in animals. This concept has important neurophysiologic implications regarding the basic mechanisms of cerebral function.[12]

Further evidence of the potentialities of depth electrography for use in the neurophysiologic investigation of interneural connections (brain pathways) has derived from the investigation by this technic of the pathways of olfaction and vision; an investigation of auditory impulses is contemplated.

To the best of our knowledge the inaccessibility of the human olfactory system has accounted for the scarcity of information relative to the response of the electro-encephalograph to sensations associated with smell. During the course of recording from the depths of the frontal lobe, it was possible for the first time to demonstrate waves related to olfaction in humans. A continuous source of stimulus was found to elicit rhythmic potential discharge, a fact which heretofore had not been encountered in humans. These findings stimulate thought and suggest the mechanism by which olfactory stimuli are centrally differentiated[13] (figure 6).

The investigation of visual pathways is discussed under the results of stimulation; as already noted, the recording of primary and secondary auditory relays is contemplated but not yet achieved. Confirmatory evidence of frontocerebellar tract connections with similar synchronous rhythms has suggested heretofore unsuspected functional electric circuits.

The electric structure of highly synchronous focal discharges in humans has been of considerable interest. The possibility of recording activity in the human brain from relatively small numbers of discharging neurons allows a method of obtaining basic answers regarding electric focal discharges in humans. The extremely high gain employed for reproduction of these discharges to date has introduced extraneous noise that clouds interpretation of the records. Evidence is presently at hand, however, that refined equipment and microelectrode technics will give valuable and

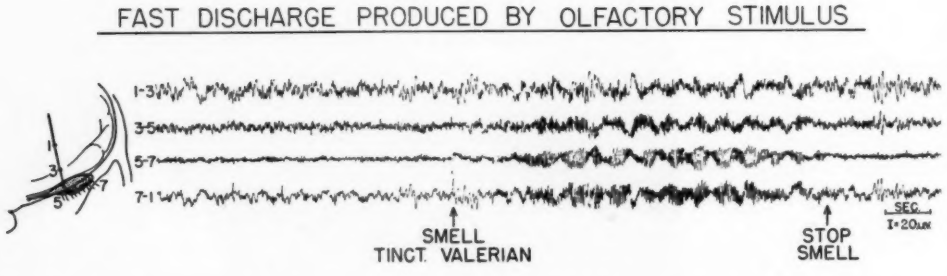

FIGURE 6. Depth electrogram of olfactory pathways at base of frontal lobes. Note the fast rhythmic discharge produced by an olfactory stimulus. The diagram to the left of the tracing is based on roentgenographic data. The left olfactory bulb is shown with the tip of the deep electrode passing underneath. The numerals 1, 3, 5 and 7 indicate the various contacts of the depth recording electrode.

valid information concerning the structure of focal neuronal discharges and other related electric phenomena in humans.

Use of depth electrodes may clarify, for the first time, some of the intricacies of human intracortical and cortical-subcortical connections of which now so little is known and yet which are so vitally important to the understanding of total cerebral function.

The anticipated future of depth electrography appears to hold much promise for the physicist and electrographer in the understanding of basic electric phenomena in the central nervous system. For the neurophysiologist, the depth lead portends to take up and proceed where neuro-anatomic and micropathologic investigation necessarily leaves off.

One of the most interesting questions related to depth electrography is concerned with the problem of mental activity and thought processes. As yet, no definite relationship between mental activity and the depth electrogram has been encountered, although the results of stimulation of the subcortex have been suggestive. More refined technics and increased future knowledge may permit some insight into the processes of thought.

The occurrence of unusual rhythms in the depths of the frontal lobes not obtained in records from the scalp or cerebral surface and seen in all psychotic patients investigated by us has been surprising. Other investigators recently have noted these heretofore undescribed rhythms in the basofrontal areas. Sparse knowledge of the pattern of subcortical activity in "normal" patients does not allow interpretation of our findings at present. However, intriguing speculation as to the possible relationship of these rhythms to mental abnormality has been raised. At present, we must be content to note their existence until our knowledge of normality will allow valid interpretation.

The presence of abnormal or changing rhythms in the cerebral depths of psychotic patients suggests that the depth investigation of other neuropsychiatric disorders may in time increase knowledge and open avenues to a more rational medical treatment and the possibility of unsuspected surgical amelioration. Those disorders which already have yielded or appear most likely to yield worthwhile information are epilepsy, psychosis, the dyskinesias (disorders of motion), mental deficiency, early stages of tumors deep in the brain, congenital spasticity and profound neurosis. There is some evidence that central potentials concerned with pain might be investigated by depth leads.

Although considerable effort and research have been devoted to investigation of epileptogenic foci on cerebral surfaces, along deep gyri and even on the insular cortex, little attention had been given to the degree of extension of these surface foci into the depths of the brain and to the equally important problem of independent subcortical firing zones causing clinical epileptic manifestations.

It was quickly noted that depth electrograms recorded surprising subcortical activity in epileptic patients. Some of these findings perhaps are illustrated best by the following case report.

Case Report

A 7½ year old white boy was first examined at the Mayo Clinic in June 1952 because of convulsions of three years' duration. Birth and development had been normal until the onset of convulsions at the age of 4½. The mother, father and one sibling were in good health; there was no history of familial disease or convulsive disorders.

The pattern of seizures described by the parents and also witnessed during examination was interesting. The child would stare suddenly and display an ashen-gray color and white lips. At first, slight movement of the left side of the face and then jerking of the left arm and leg occurred; finally the right side of the body became involved in the clonic seizures. Medication had been administered for several years on an irregular schedule.

Results of extensive general and neurologic examinations, roentgenograms of the skull and thorax, laboratory studies and psychometric tests were compatible only with the diagnosis of convulsive seizures of undetermined cause. Electro-encephalography re-

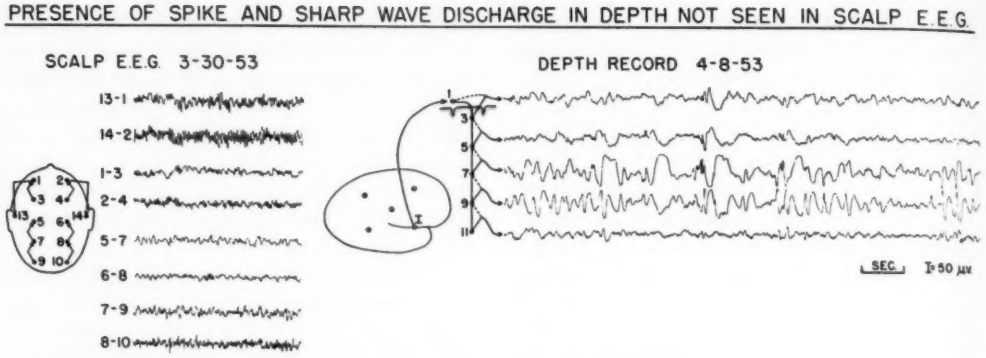

FIGURE 7. Scalp electro-encephalograms and depth electrograms recorded from a 7½ year old boy prior to operation. Note the absence of great abnormality in the scalp recordings and the presence of high-voltage sharp discharges in depth leads 1 and 3 (contact separation, 1 cm.).

vealed a right temporal dysrhythmia, but considerable discrepancy was noted between the serious nature of the seizures evidenced clinically and the rather minimal electric abnormality (figure 7). Results of diagnostic air encephalography were interpreted as within normal limits; examination of the cerebrospinal fluid was noncontributory. A planned medical regimen employing diphenylhydantoin sodium (DILANTIN® sodium) and phenobarbital was advised. The necessity of follow-up examinations at regular intervals was emphasized.

On three subsequent visits, the boy was reexamined because of the intractable nature of the seizures. Despite regulation of medication and the use of ketogenic diet and other conservative therapeutic methods, frequent convulsions persisted. In April 1953 a carotid angiogram was performed to rule out the presence of an underlying vascular anomaly. Serial electro-encephalographic tracings and activation studies with pentylenetetrazol (METRAZOL®) continued to show right-sided dysrhythmic changes with some spike characteristics but failed to demonstrate convincingly a focal character to the discharge.

Because of failure of medical therapy (he had as many as 15 separate seizures in a day), the patient's disinclination to use his left side, his inability to attend school, and his mental apathy and sluggishness, the question of depth electrography and operative intervention was entertained.

Depth electrography revealed extensive subcortical activity manifested by spike waves with four or five separate foci; the principal focus was situated in the anteromedial aspect of the deep portion of the temporal lobe (figure 7). Excision of the cortex and subcortex in the region of the principal focus was planned in the hope that the secondary foci might become quiet after this procedure, as had been noted in other cases. This operation was done in April 1953.

After operation, the previous scheme of medication was resumed. Except for three grand mal seizures early in the postoperative course, the patient has been entirely free of seizures. He was last seen in October 1953.

This case is not presented to illustrate the results of excision of an epileptogenic focus, for it is well known that several years of evaluation must precede any worthwhile observations on the value of the operative procedure. Of importance, however, is the method employed to demonstrate deep foci of epileptogenic activity when recordings from the surface were not compatible with or indicative of the extent of intractable clinical disability and did not give evidence adequate to allow considering operative interference.

The discovery of subcortical epileptogenic foci may result in the future saving of much

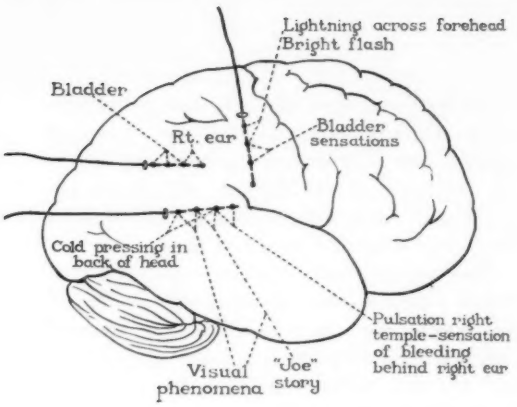

FIGURE 8. Drawing of depth electrodes and brief summary of responses elicited by stimulation of various cerebral depths in an epileptic man.

cerebral cortex. The cortex may be split and the deep focus excised, with sparing of the overlying brain. Subcortical foci may be multiple, as in the case just mentioned; when the trigger focus is excised, the secondary foci may then subside.

Quieting of multiple epileptogenic zones under depth observation has raised the question as to the true extent of such foci in records obtained in the operating room. It appears likely that irritable foci may reflect or disturb other cortical or subcortical zones. Removal or quieting of the principal dysrhythmic zone may allow many of the secondary foci to become minimally active or to subside completely. This suggests that abnormally discharging cerebral tissue that previously would have been excised may remain.

The existence of single or multiple active subcortical foci undoubtedly accounts for some of the less favorable results and uncertainties in cortical excision for intractable epilepsy in the past. There is every indication that in the future the delineation of subcortical foci may improve the surgical treatment of epilepsy. Although we fully realize the necessity of long-term follow-up in the evaluation of any operation for epilepsy, the results so far are encouraging.

Depth electrography may offer an interesting method for the investigation of certain groups of epileptic patients who are sensitive to light or in whom special stimuli, such as light, music or sensory irritation, cause seizures to occur.

Since the pathways concerned with perception of light are recognized, the problem of how and by what connections the motor components are activated by sensory stimuli, with resultant myoclonic seizures, or by what routes the so-called central integrative mechanisms may be affected to cause loss of consciousness is important. It is conceivable that use of depth electrodes may give worthwhile clues with ultimate etiologic and therapeutic implications.

Cerebral Stimulation by Depth Electrodes

Much fundamental knowledge of functional localization in the cerebral cortex has resulted from studies concerning electric stimulation made by Penfield and Boldrey,[14] Walker,[15] Penfield and Rasmussen[16] and others. Although many observations of subcortical functions in animals have been made by means of stimulation through implanted leads, there is a paucity of material concerning the human brain. Much of the functional localization in the human subcortex and basal ganglia is unknown, and depth-stimulation studies through implanted leads were undertaken with great care.[17] It is hoped that what Penfield and others have accomplished with regard to the cortex may in the future be duplicated with regard to the depths of the brain.

Figure 8 illustrates some of the responses elicited during studies of depth stimulation of an epileptic patient. Perhaps the most surprising result of such studies to date is the degree to which the subcortex responds.

Stimulation through deep electrodes implanted in various zones of the brain in different patients has produced bright lights, shooting stars, multiple and other visual sensations, homonymous colored images, turning

of the head and eyes, reproduction of epileptic aurae, clinical seizures, confusion, syncopal attacks, vesical sensations, spontaneous laughter, improved accessibility in withdrawn patients who have schizophrenia, and unusual sensations about the head and neck.

The improvement noted in withdrawn psychotic patients after minimal stimulation of the frontal lobes may be related to unusual personal attention, but it appears more likely that the stimulation mimicked the effects of electroshock therapy. This observation conceivably could have far-reaching implications toward development of a safer, less damaging and more directly effective form of electroshock treatment.

Reactivation of certain epileptic aurae with their mental associations significantly appears to be the most thought-provoking of the related findings in depth recording and stimulation. Of course, the ability to reproduce epileptic aurae and localize the deep irritative zones will aid considerably in studying the cause of epilepsy. The fact that slight depth stimulation in the posterior parietal portion of the subcortex can elicit from a patient descriptions of a scene that had occurred 30 to 35 years before with a friend named Joe has interesting implications.

It is possible that neuronal networks or circuits, if such exist concerned with memory, can be reactivated by slight stimulation. It is possible that the electric relays, the networks and the associations of thought patterns can be opened by stimulation with electric currents of graded intensity, frequency and wave form. This, of course, is speculation but from such clues have materialized medical advances.

At present, stimulation of the depths of the human brain is in its crude infancy. Even so, stimulation studies portend exciting progress in the vast uncharted functional realm of the subcortex.

Discoveries possible from studies of the subcortex, basal ganglia and brain stem in living humans appear to be limited only by the restrictions imposed by the technical equipment necessary and the imagination and ingenuity of the investigator. The prime factor in each case, however, must be investigated for the ultimate welfare of the patient. The decision as to the utilization of this new diagnostic procedure must depend on the possibility of benefit to the patient.

In two recent cases involving excision of epileptogenic foci, edema of the brain was encountered at operation. There was no clinical manifestation of this edema, and each patient had an uneventful convalescence after excision of the epileptogenic focus.

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Backache

Diagnosis and Treatment from an Orthopedic Standpoint

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The procedure and salient points in the history, physical examination and x-ray studies are presented so as to facilitate the diagnosis. Once the diagnosis is established, the recommended therapy is proposed. Myelography in the diagnosis of herniated disk is discussed and therapy for this condition outlined.

CARLO SCUDERI

THE problem of backache is open to a lot of argumentation, misunderstanding and ill treatment. At one time or another almost everyone has been bothered with backache, and almost every physician has had many patients in his office who have presented various problems associated with backache.

The problem is complicated and sometimes difficult, and it is also difficult to cover the entire field in a fairly brief discussion, but I hope to offer some ideas regarding the diagnosis and subsequent treatment of this puzzling complaint.

Most important when first seeing a patient is to take a very comprehensive history. I don't know of anything that helps more in the ultimate solution of this problem than a good, well-taken history.

The diagnosis should be made early and be accurate; the best way to reach an accurate diagnosis is to spend sufficient time on the first examination. After discussing the matter with the patient, the next question is: What are the salient points in the history that will help? There are, briefly, about six or seven conditions that cause the more common backaches. First of all are sprains and strains of the lower back. The history usually given is, "Saturday I was home and decided to clean up the basement and help my wife move a trunk around and I had a severe pain in my lower back and I could hardly sit down." There is no use discussing a brain tumor or a cord tumor or some other unknown etiologic factor in this man; the man just

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strained his back. It is certainly a very good indication for the right treatment.

Another example is that of a fellow about 18 or 20 years old, who is going to college and starts to play football. He is under rather heavy physical strain and finds that he can no longer play more than 15 or 20 minutes before his back begins to bother him, whereas formerly he never had much trouble with his back. The probable cause of his backache is a structural malformation or weakness, a spondylolisthesis or a spina bifida or a sacralization. With ordinary activity the defect didn't give him much trouble, but as soon as he started a lot of physical activity involving his back he began to have these problems. So, the young man who has never had much trouble with his back starts to have trouble when he participates in extensive and severe physical activity, and a congenital malformation is probably the etiologic factor.

Then, there is the individual, in his late forties or early fifties, who has put on a little more weight than he should and who can't run up the stairs as quickly as he could before without having to stop and pant. He now finds that when he first gets up in the morning he has a little difficulty tying his shoes, but during the day the backache seems to get better, and toward the end of the day he feels pretty good. Usually he is very much overweight and doesn't do any activity of any kind that isn't absolutely necessary to provide a livelihood. His probable diagnosis is an osteoarthritis of the spine.

There is also the individual who works in an industry and says that he was perfectly all right until he and another man tried to move a piece of machinery that weighed several hundred pounds; suddenly the other fellow tripped and released one end of the load, throwing the full weight on him, and he was seized with a severe stabbing pain in his back. After about half an hour or so he felt considerably better and went home; the next day he noticed that his backache was worse and, for the first time, he had some pain running down his leg. He found that when he coughed or sneezed or when he had a hard stool the backache and sciatic radiation became worse. If you had only one diagnostic guess—that man probably has a ruptured disk.

Then we come to the fellow who never wanted to work very hard. He has a very industrious, hardworking wife. All at once, at the firm where he is working, he does a lot of heavy lifting, develops a severe pain in his back and has trouble getting around. The boss or foreman says, "John, what happened to you?" And he says, "I strained by back." The foreman says, "Come over here and sit down a little while. Why don't you go to our nursing station and have the nurse give you a little heat on your back?" For the first time in his life someone is paying a little attention to him. He goes to the nursing service, takes off his clothes in the middle of the afternoon, puts on a loin cloth, lies down, gets heat on his back, a pretty young lady rubs his back, he gets cold water with ice in it, in the next hour 15 people ask him how he is doing, and say, "Don't hurt yourself; we'll drive you home in the company car." Well, he comes home in the company car and his wife says, "You know, John, the ashes have to be carried out," and he says, "Well, you know, I hurt my back and was told to take it easy."

"Oh, you hurt your back, you'd better go to bed." For the first time in his married life he gets supper in bed. Well, he never had it so good. The next thing you know, it keeps on for a few days and it is a man with an awfully strong constitution who says, "I want to go back and lift those hundred-pound sacks of potatoes." Let me tell you, they keep that up for a while and kind of like it.

Next, the neighbors want to know why John isn't keeping up his grass and digging in his garden. "Oh, he had an accident to his back," so the neighbors help him with his garden; he gets all kinds of help and the doctors look after him.

After a while you have a patient with a "psychosomatic back." That is a real problem! Carcinoma of the uterus or sigmoid is almost easier to cure!

After the history is obtained, the patient should be examined. It is very important that the patient remove sufficient clothing to permit a thorough examination without obstruc-

tion. In our office the men wear a loin cloth and the women wear their brassiere, panties and slip.

What should be observed during the examination? It is very important to see whether the patient has any curvatures, whether he has a list to the back, whether the muscular development is good or poor, whether there is a slouch. Notice how he walks, whether he drags his feet. Is he able to squat and rise? Test the reflexes of the extremities. It is important to know whether or not there are any neurologic changes. Certainly no patient who is a malingerer can fake the patellar or Achilles reflexes. It is also important to test the sensations of the lower legs with a pin or by stroking them with cotton to see whether or not there are any changes that follow the dermatome distribution of the nerves to the legs.

Very often in industrial cases, because of prior coaching by attorneys or because patients feel that if they are seriously injured they will be well compensated, some patients misrepresent findings. Unless a man has had some medical background or been well coached, it is very hard for him to know where the dermatome distribution to the legs is. In fact, some of us—and I include myself—should occasionally look at an anatomy textbook to see where the fourth and fifth nerve roots in the lumbar plexus run. A patient can't fake that very well. If a man claims that he has had sciatic pain in his legs for a long period of time, that he can't work and limps, and so forth, it is simple to check the circumference of both legs and note whether he has atrophy of one side. You all know that a little discrepancy between the two sides is normal, but any marked discrepancy has definite clinical significance.

It is important that the patients be observed as to whether the motions of the hips, knees and ankles are normal; that has a bearing on the case. The Lasègue test, Kernig's sign, the fabere sign, and different types of torsion tests for the back are valuable and can be reviewed briefly in any book on orthopedics.

The straight-leg-raising test is very important to tell whether the patient has any sciatic nerve irritation. The different torsion tests indicate whether there is pathologic involvement of the lumbosacral or sacroiliac joints. When notations of all these things have been made in the record, there will be a very good basis on which to make a deduction—if not at that time, then at the next examination.

If a patient is having enough trouble with his back to spend his time and his money for a medical opinion, don't let him go without getting an x-ray film; this is very important for every patient with a backache. I don't know of any luxury that is more expensive and less productive than poor films. The films must be of good quality. Every now and then films are mailed to us that must have been taken on a very cloudy day in London, because you can just see the haze of a battleship or a ship in a harbor, but aside from that you can't tell just what it is. To know if there is any arthritic lipping or any narrowing of a disk space or the possibility of a metastasis from a carcinoma, you must have good diagnostic films.

A longitudinal section of the vertebral column shows the intervertebral disks between the bones. The disks consist of fibrocartilaginous material and serve as shock absorbers. There are very powerful ligaments anteriorly and posteriorly, openings between the vertebrae through which the nerve roots run, and the ligamenta flava, which are thickened, and which are found at the operative approach to a disk just before the peridural area is reached. There are also the powerful ligaments that run between the posterior spinous processes. Altogether there is a very complicated structural mechanism in the lower back.

A degenerative disk has a tendency to penetrate posteriorly; a normal disk has the annulus fibrosus, a material that looks like raw lobster tail when you operate. The nucleus pulposus disappears in the older age group. Sometimes there is a ruptured disk in the vertebral body which usually is asymptomatic and is found in individuals who have osteoporotic spines.

The powerful ligaments in the vicinity of the sacroiliac joint connect the sacroiliac joint, the lumbo-iliac region and the lumbosacral area. With all of the ligaments in this region,

it is easy to understand that they are apt to tear under certain stresses and strains.

A top view of a typical lumbar vertebral body would show the fibrous material that forms the annulus fibrosus, the nucleus pulposus, the cauda equina and filaments, and the posterior and lateral transverse processes. The function of the intervertebral disk is to act as a shock absorber between the bones. When we are on our feet all day, we actually squeeze some of the fluid out of the disk, so that at the end of the day we are a little shorter than when we first got up in the morning. When we lie down the fluid comes back into the disk and its expands again. As our parents grew older they became a bit shorter, and a lot of that shortening was due to partial collapse and dehydration of the disks.

Some of the things to look for in x-rays are illustrated in the discussion which follows. For example, in the case of a patient who had had pain and discomfort in his sacroiliac joint for a period of about 15 years, his sacroiliac joint was very sclerotic, white and almost completely obliterated. If this continued to be bothersome, the only solution to that problem would be a surgical fusion of the joint. In this particular case the sacroiliac joints were almost completely fused from an old arthritic condition and all you could see was a roughening of the inferior portions of both sacroiliac joints.

A case that looked very simple involved a patient with a complete spina bifida. There was no posterior bony covering of the sacrum and the neural arch of the fifth vertebra was completely absent. This man has a structurally weak back and, as soon as he experiences the stresses and strains of any activity, he has progressive problems with his back. For this reason, if he avoids becoming overweight and avoids heavy work, he probably can live normally without too much difficulty.

An oblique view of the lumbar spine is necessary in cases where you expect to find a spondylolisthesis or osteoarthritic changes. In one case, the articulation at the L5-S1 level was very sclerotic, narrowed and undergoing degenerative changes. A patient with that condition may ultimately need to wear a rigid low-back support or, in rare instances, require a spinal fusion.

Another patient showed a very marked congenital malformation, with the posterior spinous process of the fifth vertebra in oblique position and with a lack of fusion of the laminae. This patient has a structural weakness of the back which, under heavy stresses and strains, will be quite troublesome.

In the only case of its type that I have ever seen, the patient had no history of any gunshot wound, osteomyelitis or operative intervention, but there was a complete absence of the articulation on one side. I need not mention that a fifth lumbar on a first sacral without any articulation, with pinching of soft tissues every time the patient bends from side to side, is certainly an outstanding condition for spinal fusion.

A particular case came to me because of an injury which the patient had received at one of the steel companies in Chicago. The x-ray study indicated that the condition present was of longer duration than the alleged nine months following the accident. I am sure that the doctor who testified that it was only of nine months' duration was not ignorant but dishonest. Unfortunately, a patient like this who gets hurt in an industrial accident always receives compensation.

Still another case involved an abnormality of the fifth lumbar vertebra, developmental in type. The fifth lumbar vertebra was much higher on one side than on the other. It had a very large interlaminal opening and a secondary scoliosis. Nature tried to develop some buttress of support but the patient had osteoarthritic changes. He came to us because of what we diagnosed as osteoarthritis of the progressive type.

A patient with far advanced osteoarthritis of the spine also had a very large spina bifida. The first and second sacral segments had no bony covering, and the posterior spinous process of the fifth vertebra was very elongated, acting something like a rudder. It does not require too much imagination to believe that when this man stooped over or moved from side to side, this "rudder" also would move from side to side and pinch the

soft tissues between the margins of the sacrum and the posterior spinous process and be a source of trouble. The preferred treatment for this patient was a spinal fusion.

In a case of a spondylolisthesis without any apparent defect of the pedicle, we thought the slipping forward was due to the fact that the articulations had worn down. There was about a quarter of an inch shift, the margins were very sclerotic and the disk spaces were narrow. This did not mean that the man had a ruptured disk with pressure on a nerve root, but rather that he had some pathologic changes of an osteoarthritic nature which had destroyed the joint and were also destroying the disk. If results of neurologic tests were negative he would not need an operation, but, if his pain continued, he probably would require some form of immobilization, either by a spinal fusion or a rigid corset.

Sacralization occurs when the transverse process of the fifth lumbar vertebra fuses either completely or incompletely with the sacrum. This usually results in a weakened back because it throws excessive strain on the opposite side, and some patients develop marked osteoarthritis of this articulation. If the symptoms are very pronounced, the only cure is a spinal fusion, not resection of the transverse process. If, once in your lifetime, you try to take out the transverse process you will never do it again, because you will be surprised to find that the transverse process is probably closer to the umbilicus than it is to the skin of the back.

A patient who had no apparent gunshot wound, osteomyelitis or trauma had a large defect in the sacrum. There were no scars in the back. He had a developmental anomaly whereby the fifth lumbar vertebra did not know whether it ought to be a lumbar or a sacral vertebra. A fusion was made on one side with compensatory scoliosis on the other.

As an example of the type of case which is important in litigation, a patient was riding on a streetcar in Chicago when it collided with a truck. Following this, the patient had some pain in his back. X-rays were taken and a cast was put on the patient for six months. A diagnosis was made of a fractured spine. The injury was not a fracture, however, but a Scheuermann's node, or lack of complete fusion of part of the epiphysial plate. It always occurs in the upper anterior region and the margins are perfectly smooth. X-rays in this case taken at two year intervals, showed no changes whatsoever in the configuration. A colleague and I testified that the condition was a congenital, developmental defect which had nothing to do with trauma. The jury believed us so well that they gave the patient $12,500.

If you observe the dermatome distribution to the nerves of the lower extremity, you will note what the nerve root pattern is to the fourth and fifth lumbar nerves, with the distribution into the foot and the back of the heel. If you check these patients with a pin, you can rapidly tell whether any alleged numbness is pathologic or functional.

If you test a tendon of Achilles by hitting it with a percussion hammer, an impulse is transmitted to the spinal cord and then transmitted through another neuron, stimulating the muscle in the leg. If there is pressure in this nerve, you have interfered with its function and the patient has changes in his reflexes. It is a very important clinical finding from a diagnostic standpoint in such conditions as ruptured intervertebral disk.

Years ago LIPIODOL® was used for myelograms, but it is much too irritating. PANTOPAQUE®, which is used now, is practically nonirritating. If Pantopaque is injected into the canal during a spinal puncture, you can tell if there is a defect on one side or the other. The accuracy of diagnosis with myelograms is approximately 85 to 90 per cent, when done by experienced physicians.

If a patient has an intervertebral disk injury, he should undergo surgery and have the disk removed. If there is any question in your mind as to whether or not he does have a ruptured disk, you should treat him conservatively by using a torso cast and immobilization for six to eight weeks, followed by physical therapy, graduated exercises and some form of salicylate therapy.

As to whether a patient should have a spinal fusion, we fuse only about one-third of our

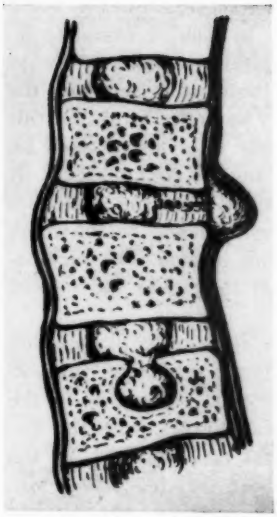

FIGURE 1. Diagrammatic illustration of three conditions of the intervertebral disk. At the top of the sketch is the normally appearing disk; in the center is a herniated disk with herniation posteriorly and pressure on the nerve root; the lower disk shows a herniation into the vertebral body—this is occasionally seen in senile osteoporosis.

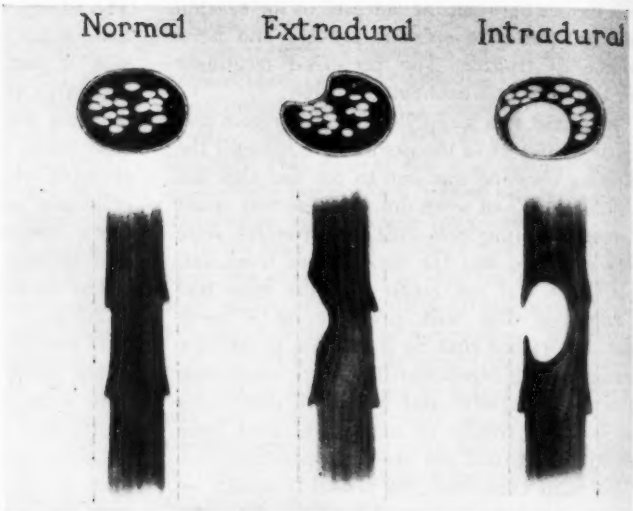

FIGURE 2. Myelogram findings in a normal neural canal, a neural canal that has extradural pressure, and a neural canal that has intradural pressure.

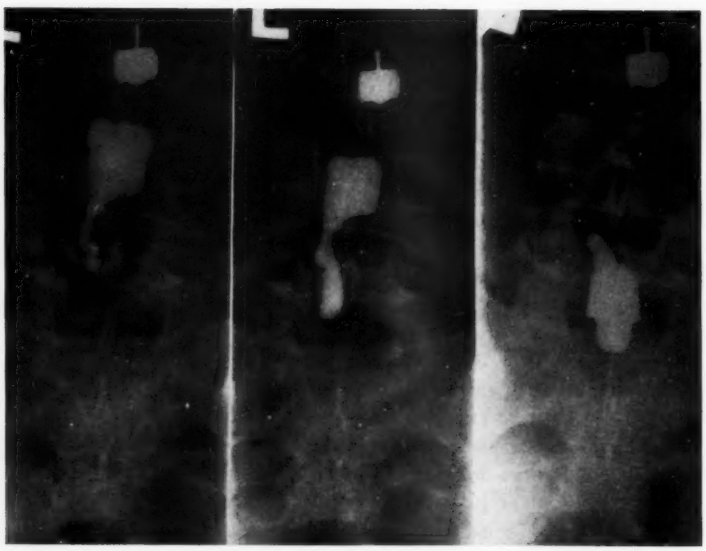

FIGURE 3. Myelogram study of a large, herniated disk at the L4-L5 level. This patient was operated on and a large disk was removed from his right side.

FIGURE 4. Myelogram defect at the L4-L5 level from which a moderate sized herniated disk was removed.

FIGURE 5. Myelogram study with a defect at the L5-S1 level. A moderate sized disk was removed from this disk space at surgery.

disk cases. If a man has a clear-cut disk with no bony changes, no spondylolisthesis, no osteoarthritic lipping and no sclerosis, we do not fuse it. If there is a spina bifida or spondylolisthesis or marginal lipping, we fuse it. If we get in and find no disk but do find something we think a fusion will help, we fuse it. (Many times we wish we hadn't.)

I wish I could tell you that every case we diagnose and operate for as ruptured disk proves to be that. Every now and then, even after all the positive clinical and x-ray findings, we operate and find there is no ruptured disk. If a man has a strained back and if you believe that there has been a tearing of the ligaments, don't put him through exercises and gymnastics. Immobilize him; let him rest and let the ligament heal. Put him in a small torso cast or a back support, but immobilize him. Don't activate him.

The osteoarthritic patient presents an extremely difficult problem. After ACTH and cortisone were released, these famous drugs cured everyone—according to the newspapers. We do not find that to be so in our office. If you can persuade these patients to lose weight, have their oral hygiene corrected, have them take salicylates and keep them from getting cold and damp, I think you have done about as much as anyone is going to do. Some of them may exhibit a phenomenal response to cortisone and ACTH.

"Psychosomatic backs" are the most difficult problems of all. I think before you decide a patient has a psychosomatic back complaint, you should examine him very carefully innumerable times and also have a neuropsychiatrist examine him. If the neuropsychiatrist agrees that it is a psychosomatic complaint, you should still have someone else examine him. More than once, some poor fellow who had a metastatic carcinoma of the lumbar spine was treated for psychosomatic disease, and I assure you that by the time you are through with a case like that you will have a psychosomatic complex and the patient will be dead.

ACTH, Cortisone and Hydrocortisone

Rationale of Therapy

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The article describes the pharmacologic and toxicologic properties of the adrenocorticosteroids, ACTH, cortisone and hydrocortisone, and stresses the importance of physiologic rationale in therapy with these potent hormones. Their clinical application, dosage and danger signals are presented in the form of tables based on practical experience rather than on controversial concepts, experimental data or an exhaustive bibliography.

CHRISTOPHER C. SHAW

In his essay entitled "The Advancement of Learning," Sir Francis Bacon in 1605 stated, "I find great repetition and but little new matter in the writers of physic." This statement is as true today as it was some 300 years ago and finds ready application in therapy with ACTH, cortisone and hydrocortisone. Current writings on this subject are so repetitious that it is difficult to determine the facts pertinent to therapy with these potent hormones on a sound physiologic basis.

Most clinical articles present lists of diseases which may be treated with ACTH or cortisone or hydrocortisone. Such lists are self-limiting and often misleading since they seldom stress therapeutic rationale. They usually omit mention of disease conditions in which these hormonal agents may be futile or even injurious. Rarely do they refer to iatrogenic syndromes and/or complications induced by the corticosteroid compounds themselves.

ACTH, the adrenocorticotropic hormone of the pituitary gland, stimulates the cortex of the adrenals to produce some 20 different steroid compounds. Of these steroids from the adrenal cortex only three or four have been isolated in pure form and studied clinically, because they alone possess physiologic, or pharmacologic propensities or attributes. Compounds E and F are the only steroids known to exert anti-allergic and anti-inflammatory effects, which account for most of their physiologic action in all but purely endocrine diseases. They also exert an electrolyte-regulating function (table 1). Another recently isolated adrenocortical steroid hormone, "elec-

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The opinions expressed are those of the author, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

TABLE 1

SIGNIFICANT ADRENOCORTICOSTEROIDS

Compound A	Inactive	11-dehydrocorticosterone
Compound B	"Mother molecule"	Corticosterone
Compound C*	DOCA	11-desoxycorticosterone
Compound D	Compound "S"	11-desoxy-17-hydroxycorticosterone
Compound E*	Cortisone	11-dehydro-17-hydroxycorticosterone
Compound F*	Hydrocortisone	17-hydroxycorticosterone

*Have therapeutic application.

trocortin," is from 15 to 30 times more potent as a salt-retainer than either cortisone or hydrocortisone.

ACTH is a water-soluble, organic secretion (a protein-polypeptide complex) from the anterior lobe of the pituitary gland where it is elaborated normally by the basophils. The regulation of secretion of ACTH is complicated but probably is controlled by means of humoral, sympathicoadrenal and/or neurohumoral mechanisms. Pituitary corticotropin stimulates the entire cortex of the adrenal gland, thus accelerating production of metabolic, androgenic and electrolyte-regulating hormones, including the salt-retaining steroid electrocortin.

Information is meager on the metabolism and excretion of the adrenocorticotropic hormone (ACTH) from the pituitary. It may be inactivated by enzymes or catabolized in the body tissues. Fifty per cent of an amount injected intravenously usually disappears from the blood stream in 5½ minutes. Prolonged therapy with ACTH will produce signs of Cushing's syndrome (hyperadrenocorticism). Conversely, if ACTH is too rapidly withdrawn after a course of therapy, the signs and symptoms of adrenal insufficiency (Addison's disease) may appear, because the normal pituitary gland becomes relatively inert during therapy with exogenous ACTH and does not regain physiologic "tone" immediately. It is, therefore, advisable to taper off dosage slowly or to increase the time interval between doses when discontinuing a prolonged course of ACTH. This will allow the pituitary gland to regain normal function and thereby stimulate the adrenal gland physiologically.

Cortisone or compound E is a steroid (11-dehydro-17-hydroxycorticosterone). It is now available in several forms for clinical application. It was first isolated in 1936 by Kendall and by Reichstein and Wintersteiner and 10 years later was synthesized by Sarett. Cortisone (compound E) possesses physiologic characteristics identical with compound F, both of which initiate complex metabolic actions on cellular enzyme systems, on electrolyte and water metabolism, and on renal homeostasis. It should be emphasized that cortisone is ineffective in modifying the acute renal lesions in glomerulonephritis, in lupus erythematosus and in polyarteritis nodosa. On the contrary, the corticosteroids may even aggravate azotemia and pre-existing hypertension. The physiologic, pharmacologic and toxicologic actions of the corticosteroids are induced chiefly by the increase of compound F in the circulating blood, whether the patient receives ACTH or cortisone or hydrocortisone.

Hydrocortisone is compound F (17-hydroxycorticosterone). It was first isolated in 1937 by Reichstein and by Mason. In 1948 it was demonstrated in the urine of a patient with Cushing's syndrome. Its beneficial effect in rheumatoid arthritis was described by Hench in 1950. Compound F is the principal hormone recoverable from adrenal vein blood, from adrenal gland perfusates and from peripheral blood. Its physiologic actions are similar to those caused by cortisone and are listed in table 2.

TABLE 2

PHYSIOLOGIC ACTIONS OF HYDROCORTISONE, COMPOUND F

1. Similar to those of cortisone.
2. Greater metabolic activity.
3. Twice as effective as cortisone.
4. Hydrocortisone acetate is only one thirty-fifth as soluble as cortisone.
5. Free compound F is as soluble as free cortisone and 14 times more soluble than cortisone acetate.
6. Free compound F is active both orally and intramuscularly.
7. Hydrocortisone acetate is inert by intramuscular injection.
8. Toxicity almost identical.
9. Absorption, intermediary metabolism and excretion of hydrocortisone parallels that of cortisone.
10. Oral hydrocortisone (compound F) more effective than intramuscular "hydrocortone."
11. Intra-articular injection of 10 to 50 gm. of hydrocortisone acetate is effective for three days to three weeks in osteoarthritis, trauma, gout, bursitis.
12. More effective in certain ocular diseases (as an ophthalmic ointment).

Indications for adrenocorticosteroid therapy are itemized in table 3. Dosage schedules cannot be categorized except on the basis of the patient's response. Suggested programs of treatment are presented in tables 4 and 5. Clinical caution is emphasized in table 6. Signs of favorable response are an increased appetite associated with euphoria, reduction of fever, disappearance of pain and inhibition of inflammation. These signs in themselves may be treacherous, since they may give the physician and the patient a false sense of security. The dangers of masking severe infection or of perforation of a peptic ulcer as the result of increase in circulating corticosteroids must not be minimized.

ACTH, cortisone and hydrocortisone have common pharmacologic actions. They are crucial mediators of essential metabolic processes, and they may be used judiciously in a wide therapeutic range. As a matter of record, they often are lifesaving in adrenal crises and in adrenocortical insufficiency. However, they also can produce severe toxic reactions which may lead to fatal complications (table 7). Moreover, they do not guarantee "biologic cure" of any known disease process but serve solely as "substitution agents." Their mode of action on inflammatory processes and on diseases of connective tissue still remains unknown. Nor are the effects of the adrenocorticosteroids on the other hormones of the anterior pituitary gland and other endocrine targets entirely clear. Presumably they depress the secretion of the follicle-stimulating hormone, the thyroid-stimulating hormone, the growth hormone and the gonadotropins. Apparently they have no specific action on the secretions of the posterior lobe of the pituitary gland. The physiologic effects on specific metabolic functions are almost identical whether one administers ACTH, cortisone or hydrocortisone. These effects apparently result from an increase in the circulating level of compound F. It is, therefore, logical to speak of them as resulting from the administration of corti-

TABLE 3

INDICATIONS FOR ADRENOCORTICOSTEROID THERAPY

1. Diseases in which these drugs may be life saving:	
a. Severe pemphigus.	b. Addison's disease.
2. Preservation or restoration of certain essential functions:	
a. Destructive inflammatory ocular diseases to prevent serious loss of vision.	b. Acute rheumatic fever with congestive failure.
3. Relief of discomfort and/or disabilities, as in:	
a. Allergic disorders.	b. Contact dermatitis.
4. Those chronic diseases in which the steroids may delay or modify destructive or fibrotic sequelae:	
a. As in rheumatoid arthritis.	b. As in acute hemolytic crisis of acquired hemolytic anemia.
5. Temporary benefit in selected lymphomas.	

TABLE 4

Forms for Administration and Suggested Dosage

ACTH—INITIAL DOSAGE

First day: 50 to 100 USP units, I.M. in 3 or 4 equal doses; or 40 to 80 clinical units of ACTH in gelatin; or 20 to 25 USP units, I.V. in 8 hour drip. Then reduce gradually each day until minimal maintenance dose is reached.

ROUTES OF ADMINISTRATION OF CORTISONE OR COMPOUND E

1. Tablets, 5 mg. or 25 mg., cortisone acetate.
2. Microcrystalline suspension, I.M., 25 mg. or 50 mg./cc.
3. Microcrystalline suspension of cortisone acetate in a phosphate buffer for topical use in ophthalmology, 5 mg. or 25 mg./cc.
4. Ophthalmic ointment, 1.5 per cent cortisone acetate in a petrolatum base.
5. Nonacetylated (free alcohol) compound of cortisone for intravenous use (100 mg. cortisone in 500 cc. saline or dextrose).

THERAPY WITH CORTISONE

First day: 150 to 300 mg. in tablets every 6 or 8 hours in individual doses, or one I.M. dose daily.
Then after clinical response is obtained, reduce gradually by 10 to 12.5 mg. daily to the lowest effective maintenance dosage.

TABLE 5

Treatment When Bilateral Adrenalectomy Is Anticipated

1. Cortisone, 100 mg. I.M. 12 hours before operation and again 2 hours before operation.
2. Hydrocortisone (or cortisone) I.V. during operation, 10 mg./hr.
3. Continue No. 2 for 4 to 6 hours after operation.
4. Postoperative day

	Mg. cortisone administered			
1st	50	I.M.	q.	6 hrs.
2nd	50	I.M.	q.	8 "
3rd	50	I.M.	q.	8 "
4th	50	I.M.	q.	12 "
5th	50	I.M.	q.	12 "
6th	25	Oral	q.	6 "

Thereafter, gradually reduce to maintenance levels of oral cortisone, from 25 mg. to 12.5 mg. twice a day.
In addition, give 3 to 6 gm. sodium chloride daily, amount to be adjusted to need of the individual.
The patient with panhypopituitarism should also receive DOCA®, testosterone and thyroid extract.

TABLE 6

Clinical Caution During a "Course" of Corticosteroids

During treatment, recommend:

1. Low sodium intake ("electrocortin" is most potent salt-retaining hormone).
2. High potassium intake: 4 to 8 gm. daily oral supplement.
3. Daily body weight; high protein diet; testosterone (linguettes).
4. Urinalysis, blood sugar and EKG: twice weekly.
5. Insulin, if necessary, to "cover" gluconeogenesis.
6. Physician to see patient at regular intervals to assess changes in patient's psyche and over-all clinical response.
7. Reduce dosage to maintenance level as soon as effect is reached.
8. Withdraw cortisone by 12.5 to 25 mg. daily; taper off slowly.
9. During the last three or four days of tapering off a prolonged course of cortisone or hydrocortisone, it is advisable to prescribe ACTH gel: 80 units, 40 units, then 20 units and finally 0 unit, in order to decrease the danger of flare-up of the basic disease.
10. Surgery may be especially hazardous in patients tapering off or just completing prolonged therapy with cortisone or with hydrocortisone. In such cases, resumption of corticoid therapy or switching to ACTH for two or three days before operation is strongly recommended.

TABLE 7

MAJOR COMPLICATIONS DURING STEROID THERAPY

1. Peptic ulceration with symptomless perforation.
2. Intercurrent infection—"silent" septicemia.
3. Severe osteoporosis—pathologic fractures.
4. Delay in wound healing (dehiscence); negative nitrogen balance.
5. Hypertension in pre-existing renal disease.
6. Increase in vascular fragility; embolic phenomena on sudden withdrawal.
7. Diabetogenic; decreased carbohydrate tolerance.
8. Spread of pre-existing tuberculosis.
9. Euphoria; hypomania.
10. Convulsions; suicide.

sone alone, since compound E induces physiologic changes indistinguishable from those produced by compound F.

Unfortunately, it is extremely difficult to measure the blood or plasma level of the circulating adrenocorticosteroids. It is thought that manifest metabolic changes are directly proportional to hypercorticosteroidemia. Two indirect methods of measurement may be employed clinically to ascertain the degree of biologic activity. One test was described by Thorn and consists essentially of an eosinopenia which, in the presence of functioning adrenal cortex, appears rather promptly after administration of corticoid hormones. A second method is based on measurement of the urinary content of 17-ketosteroids and 11-oxysteroids, since their excretion is roughly proportional to the plasma concentration of corticosteroids. It should be noted that ACTH and compound E are not secreted as such in the urine.

Nevertheless, the corticosteroid hormones exert certain common metabolic effects involving basic physiologic mechanisms and organ systems. Their pharmacologic (and toxicologic) effects are concomitant and unitarian and are not limited necessarily to a single organ or system or a specific disease process.

Indiscriminate therapeutic prescription is therefore fraught with danger. Iatrogenic "complications" may even outweigh the advantages. The ubiquitous metabolic actions of these potent hormones must be interpreted in terms of benefit and/or harm to the *total* organism (table 8). Hence, it is extremely desirable that the physician see the patient at regular daily intervals in order to assess the dynamic response of the individual. Laboratory tests and scientific observations are highly important adjuncts to therapy, but they are no substitute for careful and repeated clinical observation and appraisal.

TABLE 8

TOXICOLOGY OF ADRENOCORTICOSTEROIDS

1. Overdosage of cortisone—Cushing's syndrome.
2. Sudden withdrawal—Addisonian syndrome.
3. Overdosage characterized by: moon facies, buffalo obesity, acne, hirsutism, striae, oligomenorrhea, loss of libido, ravenous appetite, mental aberrations, increase in blood pressure.
4. Sudden withdrawal: fatigue, giddiness, exhaustion, hypotension, leukopenia, vascular collapse, fainting, coma, profound depression of adrenocortical function for 30, 60 or even 90 days.
5. Violent relapse of basic disease.
6. Danger of intercurrent infection; may be overwhelming.
7. Active tuberculosis is an absolute contraindication (except small doses of cortisone in Addison's disease).

Summary

ACTH, cortisone and hydrocortisone are challenging new therapeutic weapons which must be treated with clinical respect. They are important pharmacologic agents which may induce astounding physiologic changes in intermediary metabolism (master table 9). Overdosage or too prolonged therapy may initiate highly undesirable pathologic effects which, fortunately, are reversible on prompt withdrawal of these drugs.

Although they cannot and do not provide biologic cure for any single disease entity, in certain specific conditions (adrenal crises, acute panhypopituitarism) they may be lifesaving. In addition, they may be used as spe-

TABLE 9

SUMMARY OF SALIENT METABOLIC EFFECTS OF ADRENOCORTICOSTEROID HORMONES ON VARIOUS ORGAN-SYSTEMS AND PHYSIOLOGIC FUNCTIONS

1. *On electrolyte and water balance:* Retain sodium, chloride and water; increase excretion of potassium; reverse calcium/phosphorus ratio; expand plasma and extracellular fluid volume; increase glomerular filtration rate, renal plasma flow, clearance of urea and creatinine; increase body weight; may cause rise in blood pressure in pre-existing hypertension.

2. *On other endocrine glands:*
   a. Pituitary—inhibit production of ACTH; unpredictable action on follicle-stimulating hormone, thyroid-stimulating hormone, growth hormone and urinary gonadotropins.
   b. Thyroid—depress thyroxin formation; inhibit iodine uptake.
   c. Gonads—induce oligomenorrhea, amenorrhea, loss of libido.
   d. Pancreas—increase resistance to insulin; increased gluconeogenesis may precipitate frank diabetes; decrease carbohydrate tolerance.

3. *On peripheral circulation:* Increase capillary resistance, vascular tone, cutaneous and hepatic blood flow, splanchnic oxygen consumption, vascular fragility and atherogenesis (especially in children).

4. *On connective tissue:* Delay fibroplasia, decrease formation of fibroblasts and ground substance; cause regression of epithelial structures and disintegration of reticulum; disturb reticulo-endothelial system; inhibit granulation and formation of adhesions; interfere with protein synthesis and delay wound healing by inducing a negative nitrogen balance.

5. *On growth:* Suppress chondrogenesis and osteogenesis; antagonize growth-stimulating hormone; retard development of skin and appendages, lymphoid organs and mesenchymal tissues; suppress mitosis (as in plant tumors) and neoplasia in lymphosarcoma, cancer of skin, osteogenic sarcoma (temporary); are lympholytic in leukemia, Hodgkin's disease and plasma cell myeloma. (Huge doses of corticosteroids in pregnant mice increase incidence of congenital defects in offspring.)

6. *On gastrointestinal system:* Increase sodium and potassium content in gastric secretion and in saliva; also increase hydrochloric acid in fasting and nocturnal secretions; augment pepsin secretion (except in patients with pernicious anemia or total gastrectomy); increase the volume of gastric juice; invite aggravation or perforation of peptic ulcer; augment biliary secretion in amount and concentration; increase absorption of fat, protein and lipid in nontropical sprue (mechanism not clear); and decrease serum bilirubin in chronic liver disease.

7. *On hematopoietic system:* Cause eosinopenia, lymphopenia, neutrophilia and myeloid hyperplasia (improvement in anemia in Still's disease, rheumatoid arthritis, lupus erythematosus and pernicious anemia); increase platelets in thrombocytopenia, aplastic anemia, leukemia and lupus.

8. *On musculoskeletal system:* Increase muscle power, neuromuscular conduction and contractility in patients with Addison's disease.

9. *On nervous system:* Produce euphoria, manic-depressive reactions, excitement, restlessness, insomnia, analgesia, paraesthesias of frontal area; lower threshold to electric shock; may induce convulsions or precipitate suicide. (Electroencephalogram in Addison's disease reverts to normal on corticosteroid therapy.)

10. *On bone and cartilage:* Produce marked loss of calcium from bone followed by osteoporosis and pathologic fractures (especially if patient is immobilized by cast).

11. *On joints:* Suppress inflammation; restore electric potential; decrease temperature; increase viscosity and hyaluronic acid.

12. *On integument:* Increase capillary blood flow; skin becomes warmer, moister, thinner; patient may develop moon facies, acne, keratosis, hirsutism, sebaceous atrophy and excess pigmentation.

13. *On hypersensitivity:* Produce improvement in asthma, hay fever and allergic dermatitis; effective in blocking of antigen-antibody reactions.

14. *On mechanisms of defense:* Alter response induced by stress (infection, trauma, burns, shock, inflammation, pregnancy, repair of tissue); hence, "total adaptation" is overcompensated—inflammation disappears but microorganisms multiply; tissue repair is inhibited and wound healing is delayed. Bacteremia may run a fulminating course without fever, leukocytosis or toxemia.

cific substitution therapy in certain endocrinopathies, and their effect may be very beneficial to the patient with certain allergic manifestations. Finally, there is another group of patients with chronic disease in whom the steroids may delay or modify destructive or fibrotic sequelae, as in rheumatic fever or in rheumatoid arthritis. But their therapeutic advantages must be balanced against their constant toxicologic dangers. Physiologically speaking, for every beneficial clinical action there is a corresponding equal and opposite reaction.

The indiscriminate use of these powerful therapeutic agents, therefore, is mentioned only to be condemned.

This sketch of the corticosteroids has been presented mostly in outline for ready reference and clinical emphasis. It is recognized that such a superficial review will be subject to revision as knowledge of and clinical experience with these versatile therapeutic agents increase.

Meanwhile, the dictum of Sir Francis Bacon stands as true today as it did in 1605 when he stated, "For the subtlety and variety of the subject afford many opportunities of cure, so likewise a great facility of mistake."

Postgraduate Clinical NOTES

16. THE FACE IN DIAGNOSIS. I.

We should be more scholarly to observe the colour of our patients' eyes and hair, the shapes of their heads, the clothes they wear, the way they walk and hold themselves, how they shake hands and say good morning—and a thousand other things. This discipline indicates an alertness, an awareness, that gives the mind substance on which it may ruminate and food for thought. For it is far more important to know what kind of a patient has the disease than to know what kind of a disease the patient has. It is clinical acumen that should suggest to us in what directions we may most profitably employ our capacities. We need to know about the patient's reactions as an individual, about his environment, and about his hereditary trends. I am not thinking merely of insanity but also of psychoneurosis, phobias, obsessions, and compulsions, which can turn life into a hell both for the patient and for his family.

Pierrhos StKatsareas, *Lancet*, October 31, 1953, p. 929

Primary Closure of
Open Injuries of the Hand

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Practically all open wounds of the hand may be closed by suture or skin graft at the initial operation. This insures prompt healing, minimizes contracture and permits early function. If secondary operations are required, they may be undertaken at an earlier date.

MICHAEL L. MASON

THE general principles of the care of open wounds of the hand have been extensively presented many times and, while I will not go into them fully, the salient features of this care are: (1) adequate first aid, which is simply the application of a large compression dressing and a splint; (2) examination and diagnosis of the patient and the injury, which should consist of a history, general examination of the patient as well as of the wound, blood and urine examination and x-ray of the affected part; (3) mechanical cleansing of the wound, usually under anesthesia; (4) operation in a bloodless field; (5) excision of nonviable tissue but retention of all viable tissue; (6) deep repair as far as the condition of the wound permits; (7) closure of the wound and (8) application of a splint with the hand in the position of function under a compression dressing, except for certain very specific indications.

One element in initial care which is of prime importance in securing reactionless healing is primary closure of the wound. Various other elements of care have some bearing on this problem, either regarding methods of closure, indications for or against closure and, conversely, the need for securing primary closure, and these elements affect the carrying out of other procedures.

Primary closure may make the difference between securing a good functioning hand or a badly crippled one, between saving all possible remnants of a badly damaged extremity or losing the possibility of restoring what remains. The open wound is constantly sub-

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ject to contamination and infection; even a moderately virulent infection may be sufficient to jeopardize a functioning result.

The antibiotics are of great value in preventing the development of or combating already established infection. They do not, however, control surface contaminants nor are they a substitute for correct surgical care.

Wounds, of course, heal by scar, and the healing process starts immediately after the wound is incurred. During the first few days the healing tissues are simply an unorganized exudate. Very soon this is penetrated by capillaries and granulation tissue forms and continues to form until the wound closes. If to the mere fact of remaining open is added further irritation in the form of bacteria or chemical antiseptics, the granulations become increasingly exuberant and, as they form, the deeper layers become organized into dense scar. Not until the surface is covered with epithelium does the formation of granulation tissue cease. Hence, the longer the wound remains open the greater the amount of scar tissue, the more the impairment of function from this factor, and the greater the difficulty if secondary repairs are required. Scars of moderate extent are of little significance in some areas of the body. On the hand, however, even tiny scars may cause serious limitation of function.

Primary closure may be carried out in any wound unless invasive infection is already present or probably present or in which very virulent primary inoculation has occurred; for example, human bite injuries. It is quite possible that the older chronologic criterion of eight hours frequently may be overstepped today with adequate wound excision and under the protection of antibiotics, but serious consideration should be given wounds seen as late as 12 to 24 hours after injury. Time is still of importance, but adequate first aid, avoidance of subsequent tampering, and skilled surgical care enable the surgeon to close many wounds today that he would not have had the temerity to close 10 years ago.

Occasionally there are other conditions which contraindicate primary closure, and these concern especially the condition of the tissues themselves. When the surgeon fears that excision of tissue has not been complete, or if an injury due to explosion has occurred, it may seem wise to postpone closure for a few days. If the patient must be transported away from proper supervision for several days following operation, it may be well to leave the wound open for closure four to five days later. This practice and the conditions calling for it recall our experiences with battle casualties, conditions which are rarely duplicated in civilian practice.

There are several considerations relating to the wound, its history and nature, which have direct or indirect bearing on the matter of primary closure.

The history of the injury and its nature are quite important in considering the amount of skin excision to carry out. Obviously, the greater the amount excised the more difficult will be closure. If the surgeon knows the nature of the injury, he will have some idea as to the degree of damage of the skin. Clear-cut, sharply incised or lacerated wounds cause very little skin damage, and excision of such wound edges need be minimal; often no excision is needed. On the other hand, if the skin has been badly crushed by a heavy weight or roller, especially if the roller is hot or if a brush burn is added to the crush, it will be necessary to perform fairly extensive excision. If large flaps of skin have been avulsed and left attached by a pedicle, they may or may not survive. If the pedicle is distal, they probably will not survive, particularly if crushing injury is also present. With a proximal pedicle, survival is possible if proper aftercare is afforded the skin flaps, and if they have not been allowed to fold back on themselves under the first aid dressings. In the latter circumstance, when they are folded back, the vessels in the flap will have become thrombosed and the flap is already doomed.

Although excision is carried out in a bloodless field, there will be minute capillary bleeding from the skin, or the surgeon may observe tiny thrombosed vessels in the skin edges as he cuts. These findings will help him determine the extent of the excision.

A test which we have found to be of value in determining viability is one we have termed the blood pressure cuff test. The initial excision is carried out as extensively as appears necessary in a bloodless field secured by means of a sphygmomanometer blown up to a pressure of about 280 mm. of mercury. As soon as the excision has been accomplished, warm, moist laparotomy pads are pressed firmly against the wound, and the cuff then is released. The reactive hyperemia which occurs causes the skin to flush markedly. Pressure on the wound is kept up until this initial flush begins to subside; this will take from 5 to 10 minutes. The pads are then removed and the surgeon proceeds to catch and ligate any bleeders not secured during the excision. At this time he observes the return of circulation into the skin flaps and in other tissues which were questionably viable during the initial excision. Apparently many vessels will open up that may have been closed at the time of the injury. If color returns to these tissues or if they bleed, they are viable. If, however, the skin flaps remain blanched or the other tissues fail to bleed, excision should be carried farther back into well-vascularized areas.

Excision should be complete regardless of its extent, but unnecessary excision must be avoided. There is no skin as good as that of the hand for closure of hand wounds. Flaps and irregular, jagged wound borders, if viable, should not be excised initially but left intact until closure. They may be very helpful in finally closing the wound. If a finger must be amputated, its skin is saved to the extent of the viability for possible use in closure of the wound.

Closure of the wound may be accomplished by one of several methods or combinations of methods, depending on the situation. The most satisfactory closure is by suture, and here the surgeon will be happy to have saved tags of viable skin and flaps from amputated fingers which may be dovetailed into each other.

Where closure by suture is not possible, there are several methods the surgeon may use. The most useful and the most convenient is the split-thickness skin graft. That can be taken off with an ordinary blade if only a square centimeter or so is required; if larger pieces are needed they may be removed with any one of the various instruments for skin grafting. The volar surface of the forearm is a suitable donor site for small grafts, the thigh for larger grafts. Grafts of intermediate thickness make excellent coverage for soft tissues, but they will not take over bare tendon.

If bones, joints and tendons are exposed they must be covered with skin flaps and subcutaneous tissue carrying in their own blood supply. In a few instances it has been possible to swing a small sheet of areolar tissue across the exposed structure and to lay a split graft on the bed thus secured. This has been most often possible in the case of exposed extensor tendons. Usually, however, a skin flap is needed and this may be brought in from the side as a rotation flap or a sliding flap. The area from which this flap is shifted is then covered over with a split graft.

If a rotation flap or a shift cannot be accomplished, the surgeon should not hesitate to place the hand under a pedunculated flap on the lower abdomen. Such a method of closure is not often needed but where it is, it is most valuable in saving exposed bones and digits which might otherwise have to be amputated. The disadvantages of flaps are that they are difficult to manage if fractures must be immobilized or if other injuries necessitate holding the hand in a certain position.

Case Reports

A few illustrative cases will bring out many of the points that I have tried to discuss.

Figure 1 shows a partial amputation of the tips of the fingers without bone exposure. The defects can be closed very simply and easily by small split-skin grafts removed with a razor blade or sharp knife blade from the volar surface of the forearm. This man has had three such small grafts, one on the tip of each of the injured fingers.

In instances where there is exposure of the bone, as in the amputation of the distal end of the thumb, we must bring in skin and subcutaneous tissue; in order to do that we have

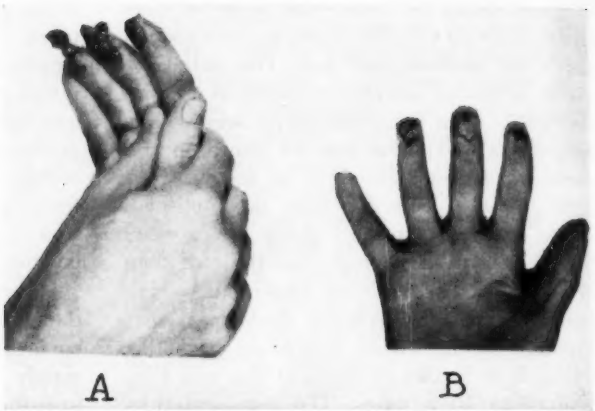

FIGURE 1. Partial amputation of the finger tips. After cleansing and excision, the soft tissue defects are closed with split skin grafts removed from the forearm. a. Before operation. b. After operation, three weeks later. Satisfactory closure was achieved for these defects.

to bring in a flap. We prefer to use the lower abdomen or the lower chest for this flap rather than to take a flap from the hand itself, although many surgeons will swing a flap from the index finger onto the tip of the thumb.

The tip of the thumb may then be covered with a flap taken from the lower abdomen. In removing these flaps we must be careful not to include too much fat; if the flap has too much fat it wobbles around and the patient is very unhappy and dissatisfied with it. If it is a fairly thin skin flap, it becomes pretty well attached—never as nice as the normal pad, but it will preserve length and give satisfactory coverage.

It is always difficult to decide whether a skin flap which may be turned back and become thrombosed will live. In a case involving a long laceration of the forearm, we found, after we let the pressure down, that the flap was viable and all of the tissues were alive. It was therefore possible to close the wound simply by bringing the tissues over and closing with a simple suture. At the same time the patient had a division of the ulnar nerve, but because of the extensive tearing of muscle the nerve was not repaired until later by exposing it posterior to the medial epicondyle, bringing it forward to secure length and suturing it underneath the flap.

In another case, the patient had an irregular, folded-back, crushed flap, and we tried to decide, when we initially saw the patient, whether the flap was alive or doomed. Unfortunately the flap could not live and it was entirely excised. There were several tendons involved and it was not possible to do a tendon repair primarily, so the area was simply covered with a large split graft taken from one of the thighs. The thin graft was later replaced by a pedunculated flap taken from the abdomen, and underneath that we were able to carry out tendon repair.

In the case of a man who had lost the skin from the dorsal surface of his left index finger, the injury divided the extensor tendon and opened up the proximal interphalangeal joint. If those structures had not been involved, an ordinary split graft would have provided very fine coverage. However, it was necessary to cover the tendon and exposed bone and joint. We repaired the tendon and the joint, and then swung in a flap from the side of the finger across that area. The defects left above and below the flap were then covered with split grafts. This procedure is called a rotation or shift flap.

The patient's final result was to have good skin over the joint and the ability to flex the finger.

Another problem concerned a man whose hand had been caught between a belt and a pulley. He not only had a crushing injury but also an abrasive burn. The little, middle and ring fingers were practically completely destroyed, two of the fingers completely ampu-

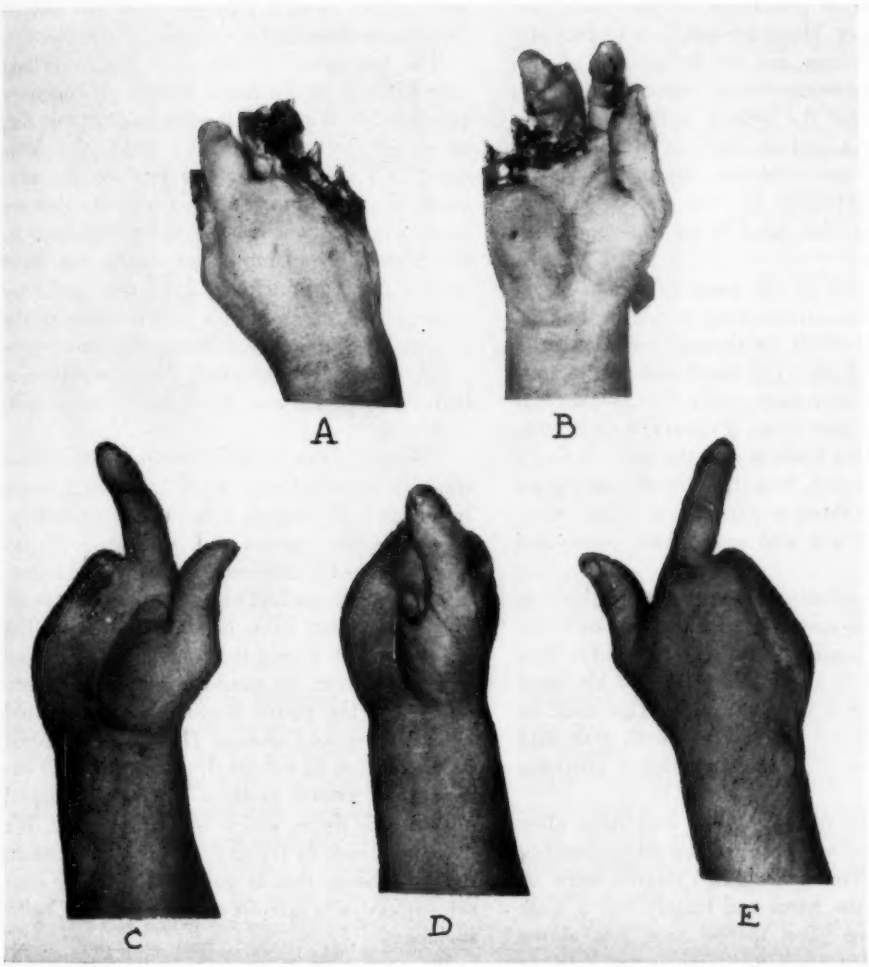

FIGURE 2. Crush burn of hand sustained between pulley and belt. Immediate pedicled flap. a and b. Before operation. c, d and e. After detachment of flap.

tated, and the middle finger was nonviable, although still present. After we had completed the necessary excision, which meant excision of tissues to the level of the metacarpophalangeal joints on both the volar and dorsal surfaces, we were left with exposed distal ends of the metacarpals 4 and 5 and part of the proximal phalanx of the third finger.

It would be impossible, of course, to cover a wound of that sort with free grafts because of the raw bone on which the grafts would have to be placed, and free grafts do not take well on raw bone. Therefore the hand was immediately put under a pedicle flap on his abdomen. The flap covered the distal end of the metacarpals and the proximal end of the proximal phalanx of the middle finger. This procedure gave the patient a useful hand and he was able to go back to work about eight weeks after surgery (figure 2).

A similar case involved amputation of the fourth and fifth fingers with exposed and de-

nuded maximal phalanges of the index and middle fingers. There are only one of two procedures that one can do in a case of this kind: (1) Amputate the remaining fingers and close over the defect, or (2) place the hand under a pedicle flap on the abdomen. In order to save the two digits, which are extremely valuable to the individual, we chose to place his hand in an abdominal flap immediately.

A volar view of the hand showed a clean-cut amputation of the ring and little fingers, and avulsion of all the tissues from the index and middle digits. The hand was placed in a flap on the abdomen, with the fingers not separated at that time. Primary healing was secured in this fashion and the patient has a satisfactory hand. Sometime in the future we may separate those two fingers, although separation would not add very much functional return.

The same principle is illustrated in the case of a man who sustained a deep burn over the back of his hand and fingers (figure 3). This man worked in a printing shop and his hand got caught in a binding press. The back of the press was hot and covered with glue, and the patient received a burn plus a crushing injury.

The patient was first seen four days after injury and we spent about two days cleaning the wound. There was third degree burn of the back of the hand and fingers and a little second degree burn in the area just above the wrist. There was no third degree loss on the palmar surface.

The patient was taken to the operating room where all of the obviously dead tissue was excised from the backs of the four fingers, as well as a strip from the back of his hand, and split grafts taken from the thigh were immediately applied to the defects.

About six days after the grafting, the area on the dorsum and the four areas on the backs of the fingers were covered with thin grafts. Long, black silk sutures were fastened along the edges of the graft, the dressing was placed on the graft and the sutures tied over the dressing to hold the graft snugly against its bed. That is the secret, I think, of getting a split graft, or any type of graft, to take—holding it down tightly against the surface.

The late result in the case just described was healing of the hand, almost by primary intention. The patient is able to close his fist, although the area over the joint is a little tight and we may have to replace the skin later. We often put grafts on initially that we know eventually will have to be replaced. In this case, for example, we could not have used a free full-thickness graft nor could we have placed the hand in a flap, because of the presence of an infected burn. However, once good healing has occurred, the thin graft can then be removed and replaced by more suitable skin.

The next case is included for several reasons. A man suffered a severe punch press injury of four fingers, resulting in open fractures, divided nerves and tendons and devitalization of a tremendous amount of tissue. If only one finger had been involved, we probably would not have hesitated to take that one finger off. Using that criterion for amputation, however, we would have had to amputate all of the man's fingers and that would have been quite a shame. Therefore, his hand was subjected to extremely careful wound excision. By wound excision we mean removal only of the tissue which is going to die. We do not necessarily try to cut out injured tissue, but only tissue that is going to die. The dorsal surface was almost as bad as the volar surface.

We were able to save the second and fifth digits and, in amputating the two central digits, we saved various flaps of skin. A flap from the ring finger was brought over onto the little finger, and flaps of skin from the middle finger were used to cover defects on the index finger. The skin flap from the palm was swung back onto the dorsum of the hand. By conserving all viable skin, we were able to get the wound closed primarily by suture alone. I don't think any split graft was used in this instance.

The patient may not have a beautiful hand, but he does have two fingers he can use, and much more quickly than if delayed closure had been practiced.

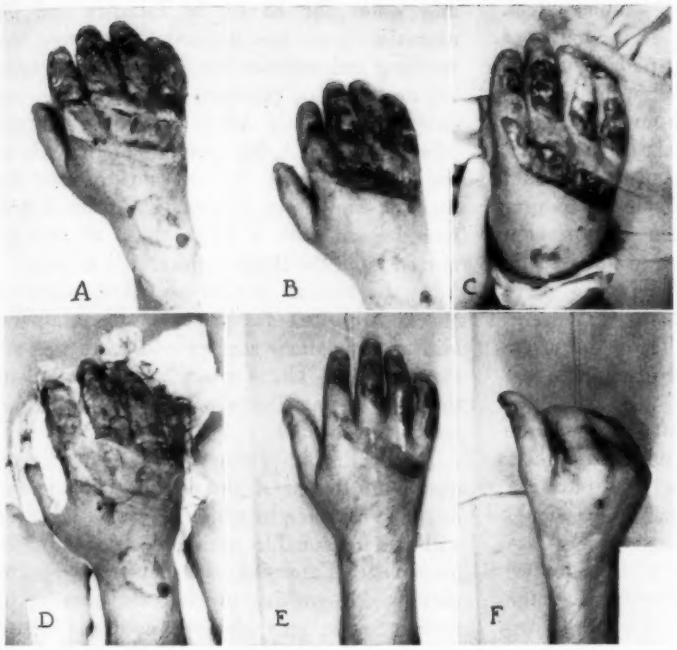

FIGURE 3. Compression burn on dorsum of hand sustained in bookbinding establishment. a. On admission four days after burn. b. One day later after cleansing. c. After operative excision of burn at time of grafting. d. First dressing, six days after grafting. The long black sutures are silk overties used to hold the initial dressings firmly against the grafts. e. Dressing removed and healing progressing. f. Hand, three months later, after the patient had returned to work.

Another problem in securing primary closure is illustrated by the case of a man whose hand was injured by an abrasive wheel which partly divided the extensor tendons of the index finger and opened the metacarpophalangeal joints. After the wound had been properly excised and the extensor tendons repaired, it was not possible to close the wound by suturing the edges across. It is obviously not feasible in such an instance to lay a split graft over the joints or over the exposed tendons. Therefore, a relaxing transverse incision was made over the back of the hand, and a double pedicle flap was shifted distally. We were thus able to close the wound by suture alone. Curiously enough, by undermining the proximal flap a little, we were then able to close the relaxing incision.

The next case is somewhat similar, the patient's wound going across the back of the hand, dividing the extensor tendons of the little and ring fingers, and opening up the metacarpophalangeal joints. It did not look like a very big wound but, after we had excised what tissue had to be removed and had repaired the tendons and joints, the wound again could not be closed by a simple suture. It likewise could not be closed with a split graft. Therefore, an accessory incision was made proximally over the dorsum of the hand and the flap was shifted distally. That still left a little defect in the web into which we placed a split graft.

In another punch press injury there was a tremendous amount of destruction of the tissues at the time of the patient's admission. The hand was washed with soap and water and the surgeon proceeded to excise devitalized tissue and to amputate those digits which had to be removed. The surgeon used some of the skin which he saved from the middle finger to close part of the index finger, but that left a large area on the dorsal surface. That wound was simply covered with a sheet of split-thickness skin taken from the thigh—the raw surface was dressed in skin.

The hand was put in a splint in the position of function and under a large pressure dressing. "Compression dressing" is perhaps a more exact term than "pressure dressing" be-

cause compression implies a gentler effect. The dressing comprises a great mass of fluffed-up gauze, abdominal pads, padding between the fingers, on the palm, and on the dorsal surface, and the whole covering wrapped snugly with a woven elastic bandage. Woven elastic is not essential but there should be a great bulk of resilient material to provide even pressure. So often compression dressings utilize the pressure of the elastic bandage, almost always creating an area of necrosis along the radial side of the second metacarpophalangeal joint. There must be lots of gauze underneath; the dressing must not be constrictive.

Shortly afterward the cleft between the thumb and index finger was deepened and a full-thickness skin graft was laid into the space to give the patient a hand which would have a grasping action.

A similar case illustrates the difficulty we sometimes have in deciding how much of the skin is viable. This again was a crushing injury of the hand with flaps torn distally over both volar and dorsal surfaces and a flap with a distal pedicle over the dorsum of the hand.

The hand was washed carefully with soap and water for 15 to 20 minutes and the necrotic tissue was excised. Sometimes this washing and excision are done without pumping up the blood pressure cuff so that one can determine exactly what tissue bleeds and what does not. A fair amount of the skin of the palm and the dorsum was excised because it would not survive. The excised area was dressed with a large sheet of skin removed from the thigh—a dressing of skin.

At the end of five or six days, when we checked the first dressing, the skin graft was laid on the palmar surface and there was primary healing. There was a little oozing along the edge. Several weeks later the hand was completely healed.

In conclusion, primary closure of an open wound of the hand should be accomplished in every instance in which the wound is seen within a reasonable period of time after its incurrence. Extensive skin loss may require various skin-grafting procedures. Invasive infection is the only absolute contraindication to securing immediate closure. Failure to secure immediate closure may destroy the only chance of providing a functional hand for the patient.

Postgraduate Clinical NOTES

17. THE FACE IN DIAGNOSIS. II.

Certain acute illnesses may be diagnosed by a glance at the face. A typical case of lobar pneumonia, for example, when the bright eyes, the malar flush (often unilateral), the active alae nasi, and labial herpes constitute an unmistakable picture—though of course in many instances of pneumonia the general appearance is far from typical. Facial erysipelas is another acute illness which permits of immediate diagnosis, as may measles, scarlet fever, and mumps. There are many other eruptions, of course, some limited in distribution to the face, some in which the face participates with the skin of the body as a whole.

Pierrhos StKatsareas, *Lancet*, October 31, 1953, p. 929

DIAGNOSTIC CLINIC

Pancreatitis

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The routine use of blood amylase determinations, day or night, in patients with upper abdominal pain unmasks acute pancreatitis surprisingly often. The goal of treatment should be to place the pancreas at physiologic rest and to insure free drainage of pancreatic juice into the duodenum. Chronic forms of pancreatitis require a variety of surgical procedures.

ROBERT M. ZOLLINGER

THE problems associated with acute and chronic pancreatitis deserve more than mere mention for several important reasons. In the first place, acute pancreatitis is a much more common disease than most physicians realize. If it is considered in your differential diagnosis and combined with a blood amylase determination on all patients with upper abdominal pain seen during the day or at night, you will be amazed how frequently pancreatitis is found. It has been our experience that its incidence surpasses that of perforated gastric and duodenal ulcer combined. Secondly, the pancreas, lying on the posterior abdominal wall, defies accurate physical examination and, like the kidney, being retroperitoneal in position, gives rise to bizarre symptomatology. It follows that inflammatory lesions of the pancreas must be considered when you are faced with abdominal distention and paralytic ileus of unexplained origin. Thirdly, it is now recognized that recurrent attacks of pancreatitis in the same patient are not uncommon and may have been unsuspected or overlooked until calcific deposits are demonstrated in the region of the pancreas during x-ray investigation for undiagnosed abdominal pain. Lastly, is the fact that mortality is high and, while the treatment of acute interstitial pancreatitis has been fairly well standardized, there is little agreement concerning the procedure of choice for handling chronic recurrent or calcific types.

Before discussing representative patients I would like to review a few basic facts con-

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TABLE 1

PANCREATITIS
CONCEPTS OF ETIOLOGY

1. "Common channel"	Calculus in ampulla
	Spasm of sphincter of Oddi
2. Duodenitis	Alcoholism
3. Trauma	
4. Relux of duodenal contents	
5. Pancreatic duct obstruction	Tumor
	Calculus
	Epithelial metaplasia

cerning pancreatitis and present several points which have proved helpful in our management of this disease.

The mere fact that we have to list five or six theories concerning the etiology of pancreatitis indicates that the actual causative mechanism is perhaps still unknown (table 1). Clinically, there are two factors that stand out as being important: (1) A large number of patients have associated gallbladder disease, and (2) too many of these patients have been a bit lenient with themselves in their use of alcoholic beverages.

The occurrence of pancreatitis has been based largely on a fact that you may recall from gross anatomy; namely, that the pancreatic juice and common duct bile frequently empty into a common channel before entering into the duodenum. A gallstone in the common channel or spasm of the sphincter of Oddi, secondary to gallbladder disease, blocks the free flow of pancreatic and biliary secretions. Under these circumstances, stimulation of the pancreas to secrete may give rise to pancreatitis. Alcohol stimulates acid formation in the stomach and, as you all know, increases the appetite. The combination of acid secretion and hunger leads to the production of secretin, which is a powerful stimulus to the pancreas. Alcohol may also be a major factor in producing obstruction at the sphincter in those instances where long-continued use has resulted in duodenitis. In addition, we should not forget that upper abdominal trauma is also a factor in pancreatitis, and it is particularly important in individuals with steering wheel injuries. Other injuries also may result in traumatic pancreatitis, and I recall seeing such problems following compression fracture of the twelfth thoracic vertebra which, as you know, is in close proximity to the pancreas.

It should be remembered that two factors must be present to produce experimental pancreatitis: (1) obstruction of the duct and (2) the pancreas must be stimulated to secrete actively. The latter of these results from food being taken into the stomach which stimulates the formation of gastric juice and, in turn, secretin. Our job, therefore, both medically and surgically, is to put the pancreas at rest; this is best accomplished by assuring oneself that the stomach is empty. Obstruction of the sphincter may be relieved by removing a diseased gallbladder or a common duct stone and may require medication to prevent or minimize spasm, so that a free flow of pancreatic juice into the duodenum is insured.

As stated originally, the pain of acute pancreatitis is often of a bizarre type and may confuse the most astute clinician. Several years ago, during elective biliary surgery, we implanted fine electrodes into the head, body and tail of the pancreas, and after the patients had recovered from their operations the pancreas was mildly stimulated in order to study the referral of pancreatic pain. When the head was stimulated, pain was evident in the right upper quadrant (figure 1). This fact does not help the clinician since there are a multitude of diseases that give similar pain distribution. When we stimulated the body, pain was referred to the epigastrium. Stimulation of the tail resulted in left-sided pain which on occasion was referred into the left flank.

The most important finding seemed to be the absence of the typical bandlike pain, which we have all read about in standard textbooks, until all three electrodes were stimulated simultaneously. It seems, therefore, that pancreatitis may cause segmental pain in the right upper quadrant, the epigastrium or the left upper quadrant, and if one sees a diffuse bandlike pain around the upper abdomen, there is every reason to assume that the patient has a severe form of pancreatitis.

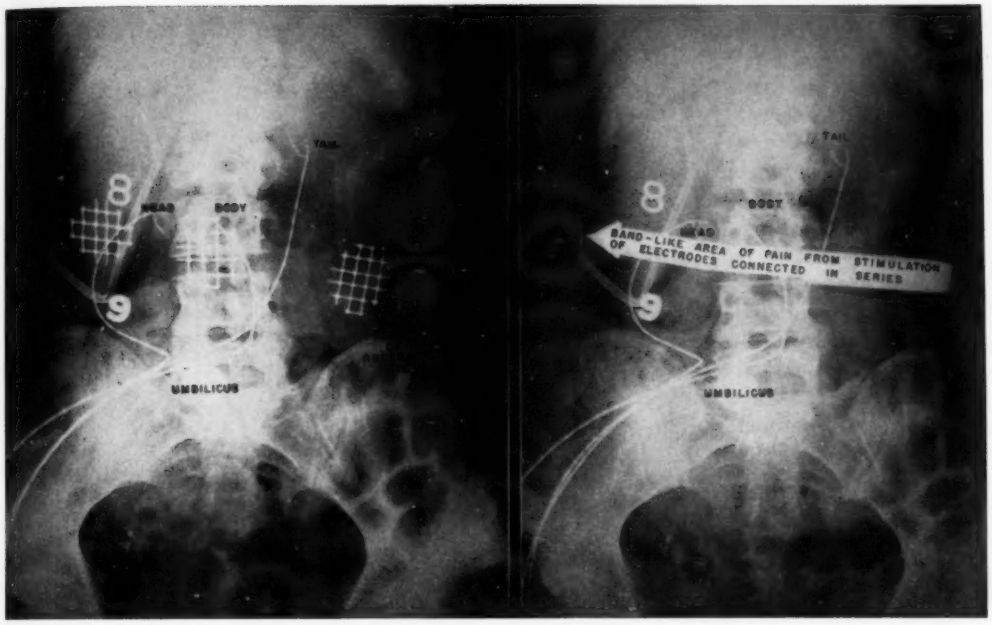

FIGURE 1. Study of referral of pancreatic pain following elective biliary surgery. When head of pancreas was stimulated, pain was evident in the right upper quadrant.

We all know that the incidence of diagnosis of pancreatitis parallels the frequency with which we think about it. Personally, I would prefer a blood amylase determination to a white blood count in patients with upper abdominal pain, since operation for acute pancreatitis contributes nothing and may add to the morbidity and mortality of the disease. Unfortunately, the blood amylase levels are only elevated for several days and usually are nondiagnostic by the third day. However, amylase values of the peritoneal fluid remain elevated for a longer period of time (figure 2). This proves useful in baffling cases of upper abdominal pain, seen some 48 or 72 hours after onset, with a normal blood amylase. In these instances you may aspirate a small amount of peritoneal fluid using a fine 22-gauge needle for amylase studies and if elevated, it proves diagnostic. We have found these miniature paracenteses helpful in solving some very baffling problems.

X-ray findings are also useful. Being a retroperitoneal organ, a diseased pancreas gives rise to paralytic ileus which frequently is segmental in type. A single gas-filled loop of small bowel in the midabdomen or left upper quadrant is frequently seen. Occasionally, gallstones are seen and should always be looked for in patients with upper abdominal pain, because of the frequent association of biliary tract disease with pancreatitis. Incidentally, this is one of the reasons for which we should urge earlier cholecystectomy in more of our patients.

Fine calcification or larger deposits of calcium in the region of the pancreas should also be looked for, and if seen in patients with suspected obstruction, it usually means that one is dealing with pancreatitis and that the obstruction is paralytic rather than mechanical. Finally, after the acute episode has subsided, one may give barium by mouth and frequently visualize a widened C loop and if a lateral view is taken, anterior displacement of the stomach may be seen. If a pancreatic cyst is present, it may be outlined with the barium. In addition, you may see a good deal

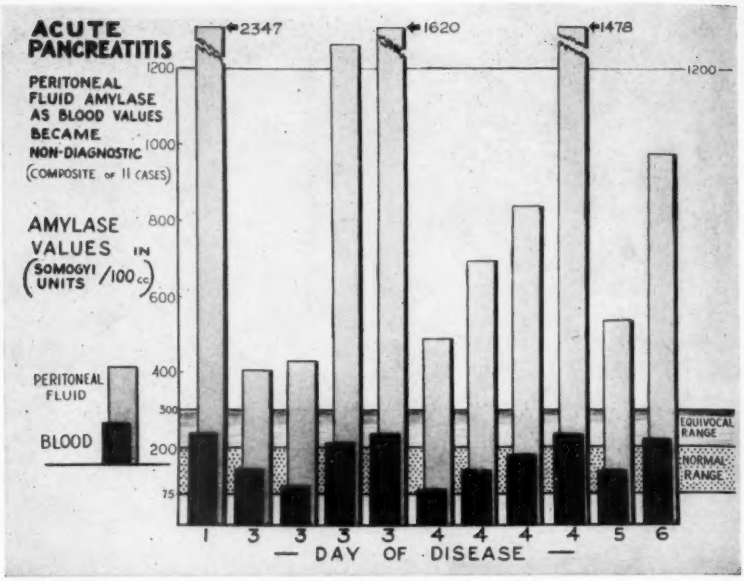

FIGURE 2. Amylase values of peritoneal fluid remain elevated longer than blood amylase levels.

of fluid in the left costophrenic angle of the chest, since there is a free communication between the lymphatics of the thorax and the abdomen. I recall a patient with this finding where a considerable argument arose as to whether the patient's symptoms were cardiac in nature. The electrocardiogram had been reported as showing a weak electropotential, whatever that might be. The patient ultimately died because of a marked hemorrhagic pancreatitis, and at autopsy there were typical yellow spots of fat necrosis over the pericardium.

I also would like to call your attention to the traumatic type of pancreatitis. I recall a patient who had been struck in the abdomen by a heavy file handle (figure 3). Apparently it had broken off while being sharpened. The patient came to the emergency room complaining of upper abdominal pain and, as is our custom, the blood amylase was measured and reported as being normal (figure 4). The patient was sent home; however, he returned that same evening with marked abdominal symptoms. At this time the blood amylase was elevated, and a diagnosis of traumatic pancreatitis was made. Since there were no signs of internal hemorrhage, the patient was not explored and his recovery was satisfactory. In this instance the blood amylase determination eliminated the necessity of exploration. Such studies must be included in all steering wheel injuries, and the possibility of pancreatitis should be considered in any trauma to the upper abdomen. The same is true postoperatively; when one sees a patient with back pain and excessive abdominal distention following upper abdominal surgery, one need not attribute the findings to leakage at the suture line until pancreatitis has been ruled out. Operations on the stomach, biliary tract and even the spleen may result in postoperative pancreatitis, which, incidentally, carries a rather high mortality.

The first patient here is a young man who, as I understand it, began having pain in his upper abdomen about three years ago. Although he was treated for ulcer during this period, two hospital admissions and numerous x-ray examinations had failed to answer the question as to whether or not an ulcer was actually present. Is that correct?

PATIENT: That is right.

DR. ZOLLINGER: Did the diet and medica-

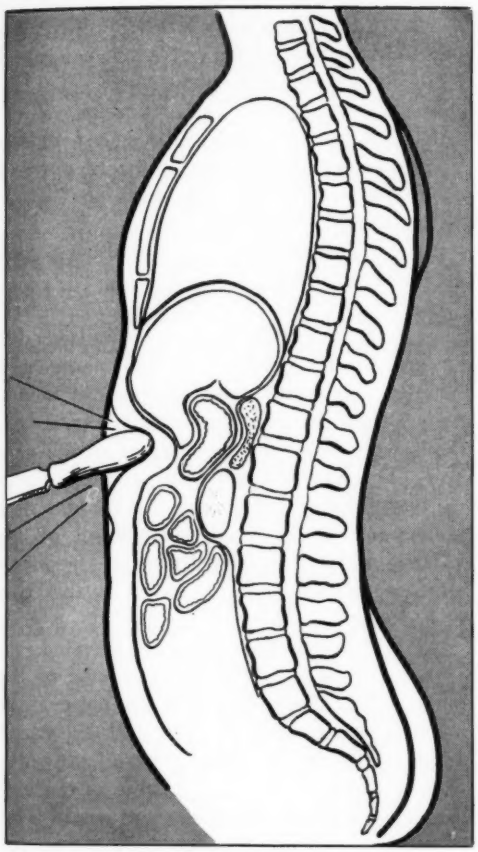

FIGURE 3. Diagram illustrating trauma to pancreas received by patient who had been struck in the abdomen by a heavy file handle.

tion for ulcer relieve this stomach pain?

PATIENT: It did temporarily.

DR. ZOLLINGER: Do you mean that diet relieved your pain at first, but that finally the pain became worse after eating?

PATIENT: Yes. After I finished eating I did get bilious gas pains.

DR. ZOLLINGER: Where did these pains occur?

PATIENT: A little off center to the left side.

DR. ZOLLINGER: Well, there are only a few things that can cause pain in the left upper quadrant, and you will recall that stimulation of the pancreas in our pain studies gave rise to segmental distribution of pain—the head to the right upper quadrant, the body to the epigastrium and the tail to the left upper quadrant. I believe this man is a rather good example of a typical case of recurrent pancreatitis, which so frequently is overlooked for a period of time. Invariably the initial symptoms seem to resemble gastric or duodenal ulcer, and the patients are placed on ulcer management. X-ray studies are questionable and the radiologist talks about antral gastritis or a deformed duodenal bulb.

The clinician as well as the patient is confused, but medical management for ulcer is invariably instituted. The ulcer diet usually means a high caloric intake and includes milk

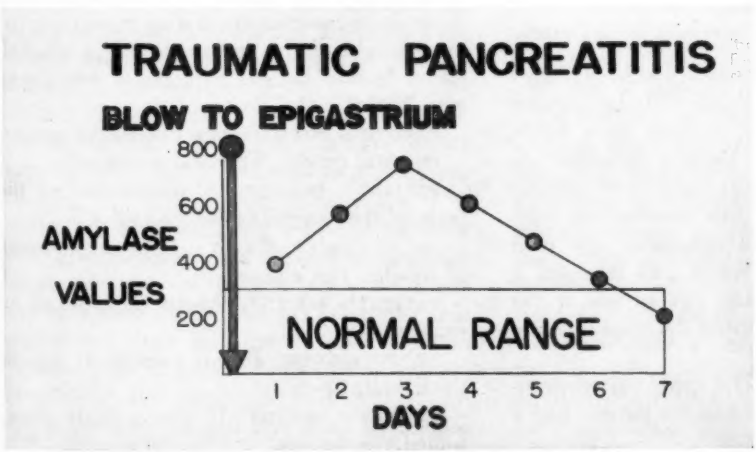

FIGURE 4. Blood amylase determination of patient referred to with figure 3.

and cream, which are powerful stimulants to the pancreas. If the patient has had pancreatitis, he soon begins to have pain; if he has pain he stops eating; when he stops eating his weight goes down, and, as in this instance, a great deal of weight may be lost. It seems, therefore, that this patient was treated for ulcer; the treatment, however, instead of making him better made him worse and he learned to avoid pain by not eating.

Now, your pain was centered on the left?

PATIENT: Yes, sir.

DR. ZOLLINGER: I would suspect that the blood amylase had not been determined during his two hospital admissions, and for this reason the blood amylase should be studied as routinely as most of us do the white blood count. In this instance, a blood amylase study would have established the diagnosis of pancreatitis three years ago rather than now at the third hospital admission, when the patient was admitted with severe pain, considerable weight loss and was found to have a large mass in his epigastrium.

We have two things to consider as far as etiology is concerned in this man. Let us see into which category our patient falls. Does he have gallbladder disease or does he partake of a little too much alcohol in some form? How about this, son? Have you ever had an attack of gallbladder disease or has your skin ever turned yellow?

PATIENT: No.

DR. ZOLLINGER: Do you drink anything other than milk?

PATIENT: Yes.

DR. ZOLLINGER: As I recall, you have tended bar on week ends and incidentally have drunk up some of the profits. In turn, pain would begin on Monday or Tuesday morning. At least, the patient had been rather free with his alcoholic intake and this resulted in pain several days later. But remember, the pain was in his left epigastrium and this was a little difficult to explain. Let us see if the x-rays help us. What about the upper gastrointestinal series?

PATIENT'S DOCTOR: The upper gastrointestinal series was negative and the patient had a visualizing gallbladder.

DR. ZOLLINGER: This information leaves me out in the open, doesn't it? But you could feel a mass in the left epigastrium?

PATIENT'S DOCTOR: Yes, definitely.

DR. ZOLLINGER: I made the statement earlier that pancreatitis defied outward physical examination. What do you weigh now?

PATIENT: 112 pounds.

DR. ZOLLINGER: And you are about 5 feet, 10 inches in height?

PATIENT: 5 feet, 10½ inches.

DR. ZOLLINGER: By insurance standards this patient should probably weigh about 170 pounds. This means that he is some 50 pounds underweight, which is commonly seen in patients with inflammatory diseases of the pancreas. The gastrointestinal series failed to help us, there was no gallbladder disease and, as I understand it, he had visualization of his kidneys with no renal pathology. The blood amylase, however, was elevated. Is that correct, doctor?

PATIENT'S DOCTOR: Definitely elevated.

DR. ZOLLINGER: With the presence of the mass, and remembering that the patient can localize pain to the left side, with the blood amylase elevated, I think it would be worth while to explore this man in spite of the normal x-ray findings. Certainly you would want to know whether he had any biliary tract pathology which had not been demonstrated by the cholecystogram; however, the x-rays appeared to show a good, functioning gallbladder. It would seem, therefore, that we have an example of pancreatitis arising from repeated overstimulation by means of ethyl alcohol, and I believe he was explored a few weeks ago. Is that right, doctor?

PATIENT'S DOCTOR: Yes, two weeks ago.

DR. ZOLLINGER: What did you find?

PATIENT'S DOCTOR: A pseudocyst of the body of the pancreas near the tail.

DR. ZOLLINGER: Was it as large as an orange or smaller, like a lime?

PATIENT'S DOCTOR: About the size of an orange.

DR. ZOLLINGER: Did it present a thin or thick wall?

PATIENT'S DOCTOR: It was a fairly thick-walled cyst.

DR. ZOLLINGER: As I recall, you accomplished drainage through this wall?

PATIENT'S DOCTOR: Yes, we placed a drain in the cyst cavity which was brought out through a stab wound in the abdominal wall.

DR. ZOLLINGER: Has the drain site healed?

PATIENT'S DOCTOR: Yes.

DR. ZOLLINGER: Are you relieved of the pain which brought you to the hospital? Do you have any trouble eating?

PATIENT: I don't seem to have any trouble.

DR. ZOLLINGER: Do you have any pain at all?

PATIENT: No pain like I used to have.

DR. ZOLLINGER: Of course, trying to evaluate the outcome of this disease based on two weeks' observation is like pouring a glass of water in the ocean and expecting the shoreline to advance.

I would certainly agree that drainage of the cyst was the simplest and most ideal procedure, since these cysts tend to communicate with the main pancreatic duct. Some clinicians have advised splitting the papilla of Vater and inserting a small catheter through the pancreatic duct. In the first patient presented, the cyst was left alone and it melted away without the necessity of operation. However, I think this patient had sufficient pain to make drainage a necessity.

The important thing to remember is that the patient is not necessarily cured of his pancreatitis. The cyst has been drained. However, considerable fibrosis and scarring remain and he may have further difficulty. I am sure he has taken the pledge to change occupations. Is that not correct?

PATIENT: I do other work besides tend bar.

DR. ZOLLINGER: Well, son, you have to stay away from alcohol if you wish to avoid more trouble.

The question naturally arises as to what type of management will prevent or minimize future difficulty. In the first place, he should stay on a strict ulcer diet so as to depress acid production, since acid gastric juice leads to the formation of secretin, which is a powerful stimulus to the pancreas. Milk and cream should be omitted and one must be careful not to force-feed these patients, although he should have enough calories to gain and maintain a proper weight. PRO-BANTHINE®, calcium carbonate, or any one of a variety of drugs may and should be used, and it should be remembered that such medication will be required for a long period of time.

The next patient is a man 78 years of age who told me that he never knew he had a stomach until a recent episode of vomiting and stomach pain following a heavy meal of fried chicken. Where was your pain at that time?

PATIENT: High in my stomach.

DR. ZOLLINGER: Did you vomit a great deal?

PATIENT: Yes, sir.

DR. ZOLLINGER: Did you have pain in your back?

PATIENT: I don't recall that I did; all of the pain seemed to be centered in my stomach.

DR. ZOLLINGER: Was it the worst pain you ever had?

PATIENT: Well, I had ptomaine poisoning some 20 years before and the pain was so similar that I was sure I had ptomaine again.

DR. ZOLLINGER: What did you do about it? As I recall, you did not see a physician.

PATIENT: That is right—I just stopped eating.

DR. ZOLLINGER: You didn't eat?

PATIENT: I was on a trip into Michigan at the time, somewhere north of Whitehall, and I decided to wait until I got back to Chicago.

DR. ZOLLINGER: I assume that this ride was pretty rough. Did you feel bloated?

PATIENT: Yes. I rode lying down in the back seat of the car while someone else drove.

DR. ZOLLINGER: This went on for a number of days, and it was of some interest in taking this man's history that he began to feel better as soon as he quit eating; in other words, he placed his own pancreas at rest. Whenever the patient ate, his pain would then recur. I think it is very important to remember that the pancreas must be maintained at rest and that in addition to assuring acid depression, food should be withheld for as long as three or four days after the patient's symptoms have subsided.

Reaching Chicago, he came into the hos-

pital where x-ray studies suggested a diagnosis of gastric ulcer. Several days later he had difficulty passing his urine and ended up having a transurethral prostatectomy. I would suspect, although I do not know this to be true, that the patient had been placed on BANTHINE® following the ulcer diagnosis and, although this was good for his pancreas, it was bad for his prostate.

While recovering on the urologic service, severe pain once again developed in his epigastrium and this time it was much worse. Vomiting was marked. A gastrointestinal series at that time showed a rather narrow stomach, suggesting external encroachment. The dilated loops of small bowel suggested paralytic ileus. At this time a mass was discovered in his epigastrium. An attempt was made to visualize the gallbladder, but since no gallbladder shadow could be seen, we must assume that it was nonfunctioning. In this instance alcoholism played only a limited role. The nonfunctioning gallbladder did lead me to presume that he had a diseased gallbladder. These facts, combined with the distortion of the lower end of his stomach and a large C loop, certainly point toward pancreatitis. It should be remembered that involvement of the body or tail of the pancreas does not give such distortion and our first patient fell into this category. The pain and finding of a mass led to his operation and, as you will recall, the gastrointestinal series failed to help the clinicians. Perhaps we should depend more on our hands than on the x-ray examination.

Did you set about to drain his cyst, doctor?

PATIENT'S DOCTOR: Yes, he was operated in December 1952, at which time a large pseudocyst of the pancreas was found presenting through the left omentum.

DR. ZOLLINGER: I interpret this as meaning that the cyst was located in the head of the pancreas.

PATIENT'S DOCTOR: Yes, it was in the head of the pancreas.

DR. ZOLLINGER: Was it a large cyst?

PATIENT'S DOCTOR: Yes, approximately 500 cc. of hemorrhagic fluid was drained from it.

DR. ZOLLINGER: That is a large cyst.

PATIENT'S DOCTOR: Four weeks after surgery the drainage ceased and two weeks later, in February 1953, a polyethylene tube or catheter was placed into the sinus tract and LIPIODOL® was injected. A simultaneous gastrointestinal series was accomplished.

DR. ZOLLINGER: Reviewing these films certainly proves that you have been successful in overcoming his pyloric obstruction and the C loop is much smaller. Remember that the tail and body of the pancreas may be removed if cysts or calcific involvement are present. Cysts in the head of the pancreas, on the other hand, are much more difficult problems and if removal is attempted, a complete pancreatectomy is usually necessary. I believe most surgeons are quite hesitant to carry out such a radical procedure. I think it was quite right that this cyst be drained to the outside.

One objection to external drainage is based on the fact that a few patients continue to drain pancreatic juice for long periods and, as in this man, the fistula becomes quite aggravated. If a quart or more of pancreatic juice is lost every day, fat absorption is so diminished that the patient may become a nutritional problem. However, this is not true in most cases and is relatively insignificant.

Anastomosis of the cyst to the jejunum or the stomach has been proposed, but I have always been a little hesitant to do this. Preferably, I like to insert a drain or catheter until the patient is improved and then wait for future developments. This is a relatively small cyst cavity at the present time, and I am rather surprised that injection of this cyst with radiopaque material does not give complete visualization of the main pancreatic duct, since a polyethylene tube placed in the pancreatic duct at the time of operation can be shown to communicate with the cyst in most instances.

Does diet improve the amount of drainage?

PATIENT'S DOCTOR: Apparently not. Furthermore, Banthine does not decrease the fluid drainage. It should be pointed out, however, that the patient has had no subjective symptoms, and his only complaint is the slight discomfort in connection with the drainage through the fistula.

DR. ZOLLINGER: The loss of only an ounce or so each day should not concern us too much, and I certainly doubt if the cyst is sufficiently large for us to consider removal. Of course, we must remember that this man has a nonfunctioning gallbladder, and the possibility of removing his biliary tract disease has to be considered. On the other hand, it has not bothered him too much and I believe he looks good for his 78 years.

I would again like to emphasize the treatment of pancreatitis. Almost everyone agrees that medical management designed to put the patient's pancreas at rest is ideal (table 2). As physicians, our first job is to relieve pain. For these patients DEMEROL® must be used and morphine should be avoided. If the pain is difficult to control, splanchnic block may be utilized. Some clinicians have gone so far as to leave a small ureteral catheter in the spinal canal, permitting intermittent spinal anesthesia. As a matter of fact, we have not found it necessary to use splanchnic blocks in recent years, since more attention has been paid to putting the pancreas at rest. Gastric and pancreatic secretions may be depressed with atropine, Banthine or Pro-banthine. These drugs not only decrease the ability of the stomach to make acid, but at the same time have a direct effect on the pancreas.

Antibiotics may be of some value; at least everyone uses them and no harm results.

Blood volume determinations have shown that plasma and red cells are lost from the circulation in patients with pancreatitis. A considerable portion of this plasma probably is accounted for by the marked edema in the retroperitoneal tissues. It follows that these patients require some type of colloid, whole blood or even one of the plasma substitutes to control their tendency to go into shock.

It has been recommended that they receive human serum albumin and that this albumin might have some antitryptic effect. It is our experience that serum albumin is worthwhile, that it does result in a shift of fluid into the plasma, and perhaps it has a beneficial effect by minimizing the edema of the pancreas itself. We have been unable to demonstrate any antitryptic effect in the laboratory.

TABLE 2

TREATMENT OF PANCREATITIS
(Initial—Conservative)

1. Pain relief
   Demerol—not morphine (vagotonic)
   Sympathetic blocks
2. Reduce pancreatic secretory activity
   Gastric suction
   Atropine—Ephedrine
   Banthine
3. Combat infection and peritonitis
   Antibiotics
4. Combat shock *(if present)*
5. Correct chemical derangement
   Hyperglycemia—insulin
   Hypocalcemia—calcium gluconate

Insulin may be required. However, one must remember that injection of insulin is in essence the Hollander test for complete vagus section and if hypoglycemia results, a considerable amount of free acid is formed which, in turn, stimulates the pancreas. The giving of insulin to a patient with pancreatitis, therefore, should be done with extreme caution.

Calcium gluconate should also be administered. We tend to give 1 gm. each day, particularly to those patients whose blood calcium level has fallen below 9 mg. per cent. If this value falls below 7 mg. per cent, there is a good chance that the patient will die.

An x-ray of a man weighing some 225 pounds who was admitted with the diagnosis of small bowel obstruction is shown in figure 5. His temperature, pulse and respiration were elevated and his abdomen was tender and silent. As is our custom, we obtained a blood specimen for amylase examination and this was reported as being markedly elevated. Incidentally, his peritoneal fluid, obtained by a paracentesis, also showed a marked elevation of his amylase content. The scout film of the abdomen revealed the picture seen in intestinal obstruction; however, calcification was observed in the region of the pancreas. A story of a previous hospitalization for undiagnosed abdominal disease one year previously was obtained. The patient was quite ill at this time and remained in the hospital a

FIGURE 5. X-ray of a man weighing about 225 pounds who was diagnosed as having a small bowel obstruction.

total of 17 weeks. His initial management included medication and diet to place the pancreas at rest. This was not hard to do, since each time the patient attempted to take food his pain recurred. During a one month interval 50 pounds of weight were lost. At that time the patient returned to the hospital for exploration. A diseased gallbladder with its contained stones was removed, and a large cyst in the head of the pancreas was drained to the outside, using a mushroom catheter. Considerable relief resulted from this procedure and, at the present time, the patient has returned to work.

Another patient had advanced chronic pancreatitis resulting from, or at least associated with, marked alcoholism. He had lost about 45 pounds of weight, was deeply jaundiced and gave a long history of epigastric pain and ulcer therapy. He stated that he had been discharged from the army with a diagnosis of ulcer, and I am sure he would rather have remained in service a few more years than to have developed pancreatitis. Like the first patient we showed, he was unable to work, finally became jaundiced and presented himself as a real problem. The calcification in his pancreas can be seen in figure 6. Incidentally, he is a mild pancreatic diabetic.

We have attempted to place this man's pancreas at rest by sectioning the vagus nerves, which of necessity included a gastroenterotomy (figure 7). A common channel, demonstrated by operative cholangiography, was bypassed by means of a cholecystojejunostomy.

Subtotal gastric resection and vagotomy have also been utilized to control acid and, in turn, pancreatic function (table 3). Splanchnic resection or sympathectomy has also been employed to control pain, but it should be remembered that these procedures have no effect on the diseased pancreas itself. Other

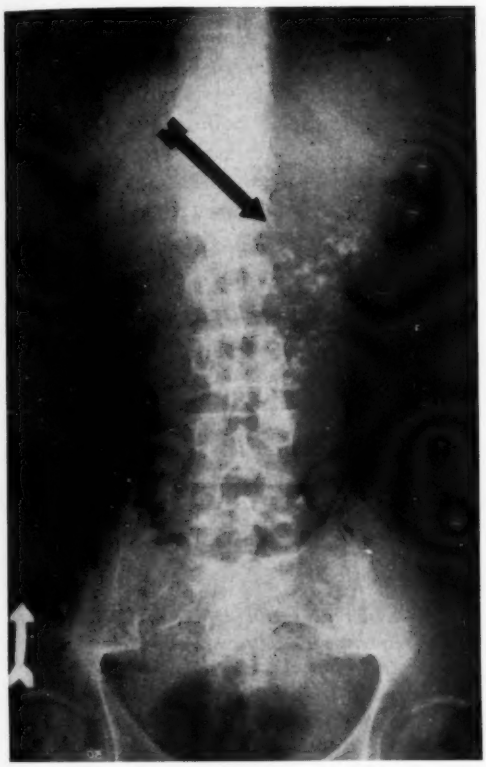

FIGURE 6. Calcification of pancreas.

TABLE 3

CHRONIC PANCREATITIS
SURGICAL MANAGEMENT

1. Remove biliary tract disease
2. Promote free pancreatic drainage
   Section of sphincter of Oddi
3. Drainage of cysts
4. Decrease pancreatic secretions
   Vagotomy + gastric resection or gastroenterostomy
5. Resection (partial or total)
6. Bypass "common channel"
   Choledochojejunostomy, etc.
7. Control of intractable pain
   Sympathectomy

measures include sectioning of the sphincter of Oddi and, finally, subtotal or total pancreatectomy. A variety of procedures, therefore, have been proposed for the treatment of these chronic types of pancreatitis, but none too successfully. The principles to remember include: First, remove biliary tract disease, and second, keep the pancreas at rest. Finally, I believe it is important to us as surgeons to view the situation of chronic pancreatitis with great humility.

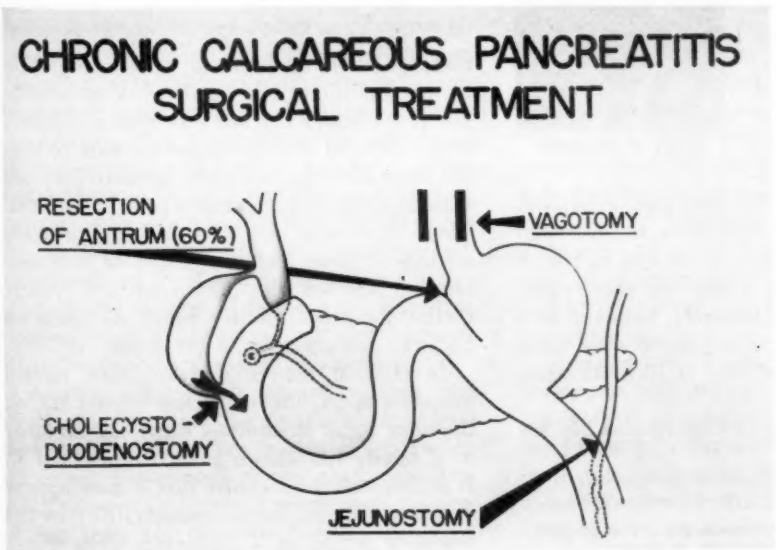

FIGURE 7. Same patient referred to with figure 6. Patient's pancreas has been placed at rest by section of his vagus nerves and gastroenterotomy.

DIAGNOSTIC CLINIC

Mucoviscidosis
Its Clinical Aspects and Treatment

EARL H. BAXTER*

Ohio State University College of Medicine, Columbus

An increasing incidence, or at least more frequent recognition of mucoviscidosis requires that the physician watch for evidence of the disease. Early recognition of the condition is imperative if proper management of the patient is to follow. Symptoms, diagnosis and treatment are discussed and illustrative cases are presented.

EARL H. BAXTER

MUCOVISCIDOSIS or, as it was formerly known, fibrocystic disease or cystic fibrosis of the pancreas, has come to be recognized much more frequently than it was previously. It has been found that something like one out of every 600 or 700 infants shows some evidence of being affected with this condition.

Before the days of antibiotics, the life span of children who had this disease was measured in months or, at most, a very few years—perhaps only one or two. Recently, however, as a result of good treatment and supervision, some of these children have lived to 18 to 22 years of age.

Since the hope for any prolonged life for these children depends on early recognition of the condition, it is worth while to emphasize it to doctors who see very young children. Irrespective of whether or not we want to handle these children, we must, because they are with us and require certain types of treatment. Those of us who may have been unfortunate enough to have had a member of our own families afflicted with the disease will readily realize the responsibility which devolves on both the parents and the physician.

In view of the familial tendency toward mucoviscidosis, the physician should be on the alert for it in siblings when one member of a family has shown some evidence of it. It is also well to recognize that it does appear in three different forms, namely, (1) in the newborn period as a meconium ileus where

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Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

it produces symptoms of acute intestinal obstruction and demands surgical treatment either by removal of the inspissated meconium or by instillation of trypsin into the intestinal tract which will produce solution of the meconium; (2) as a respiratory form, and (3) later, or early, as it may be, in the celiac form. There also may be a combination of these last two types.

Because meconium ileus primarily occurs in the newborn period and requires an emergency type of treatment, I believe that we can devote the bulk of this discussion to a consideration of the last two types.

SYMPTOMS

Poor feeding history
Repeated respiratory infections and prolonged coughing
Emphysematous chest—persistent rales
Poor nutrition
Excessive perspiration with high salt content—"Salty heads"

The condition may begin very soon after birth, but it is most commonly recognized near the end of the third or fourth month, with evidence of bronchitis or bronchiolitis, after which the child has a persistent type of spasmodic cough and repeated respiratory infections with prolonged coughing. This cough lasts after the infection has cleared up and somewhat resembles whooping cough. I can remember, years ago, treating these children, not knowing that it was fibrocystic disease or mucoviscidosis, and finding that the children had whooping cough year after year if they succeeded in living two or three years. Previous to this, however, the child is very likely to have been a difficult feeding case, necessitating one change of formula after another without very much success in development. There is always a slow gain in weight.

After a considerable period of time, the child recovers from the attack of bronchitis and seems to progress moderately well, when there are recurrences of the chest infection. Each recurrence becomes worse than the preceding one, accompanied practically always by fever and some evidence of bronchopneumonia. The loss of weight continues or the weight remains stationary and, if the child is untreated, death will result in varying periods of time.

It has been found that these children perspire much more profusely than the average, and the sweat contains a high content of sodium chloride. This was a symptom that was found by parents, or mothers particularly, who told us that when they kissed the tops of the babies' heads there was a salty taste, so there arose the name "salty heads" for these babies. When a mother tells you that her baby's head is "salty," don't laugh at her—something is seriously wrong.

After some months these children may develop a celiac type of disease with foul, bulky stools. However, the stools do not necessarily contain undigested starch, as is the case in true celiac disease.

After an interval of a few weeks, the child shows some evidence of an emphysematous chest with persistent rales.

X-ray examination usually shows some evidence of emphysema; there will be a depression of the leaves of the diaphragm with one or two more interspaces showing than is the rule (figure 1).

At some time in the course of the disease there is usually evidence of bronchitis with congestion of one or both of the hilar regions of the chest (figure 2). This is especially true whenever the child develops one of the recurring attacks of bronchial infection.

In a very young infant there is likely to be some evidence of atelectasis, usually in the upper right lobe (figure 3). Atelectasis has been seen so frequently in our hospital that when our radiologist sees it, he makes a diagnosis of suspected fibrocystic disease even before any laboratory or clinical findings have become apparent.

The emphysema increases as the fibrosis progresses, and more and more of the lung is involved by succeeding attacks of bronchitis and pneumonia (figure 4).

As the respiratory factor becomes worse, these infants and children are likely to develop a cor pulmonale (figure 5) and exten-

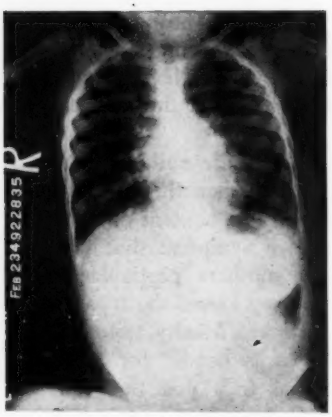

FIGURE 1. Pulmonary emphysema with depression of the leaves of the diaphragm, barrel-shaped chest and bulging interspaces.

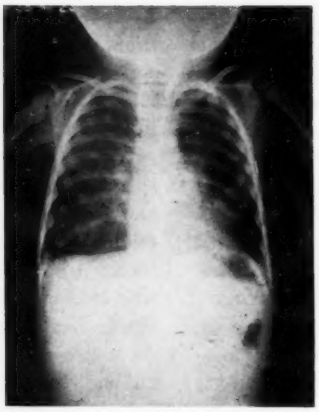

FIGURE 2. Hilar involvement in recurrent bronchitis.

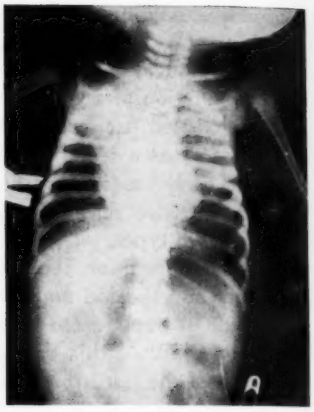

FIGURE 3. Atelectasis of upper right lobe.

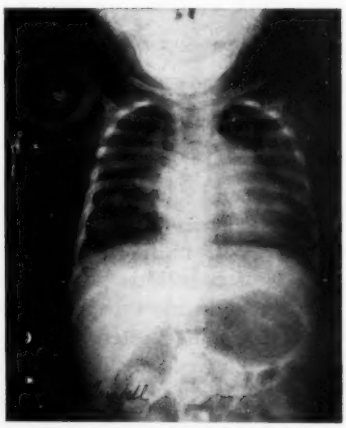

FIGURE 5. Cor pulmonale in a case of mucoviscidosis.

FIGURE 4. Fibrosis and bronchiectasis as caused by mucoviscidosis.

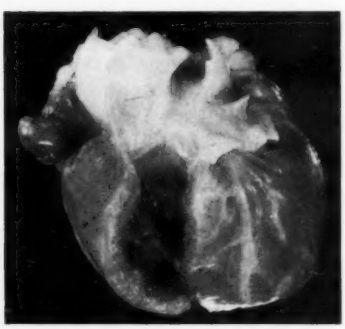

FIGURE 6. Hypertrophied right ventricle in cor pulmonale.

FIGURE 7. Emphysema in a 17 month old child.

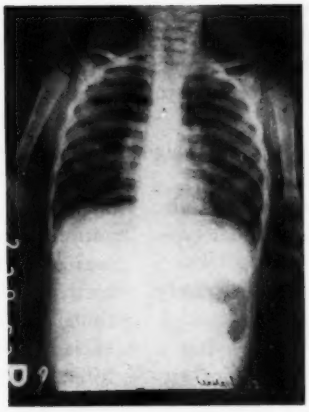

FIGURE 8. Same patient as in figure 7 at four years of age. There is now more extensive emphysema and hilar involvement.

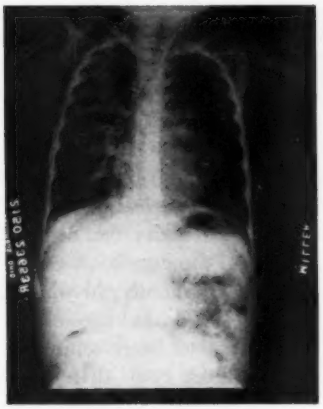

FIGURE 9. Mucoviscidosis in a six year old girl.

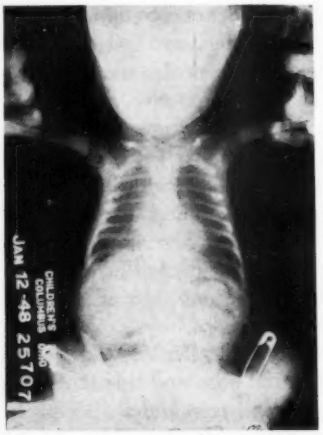

FIGURE 10. Atelectasis of lower right lobe in a two week old infant. This was a proved case of mucoviscidosis.

FIGURE 11. Same patient as shown in figure 10. Cysts were found in the pancreas and there were abscesses in the lung.

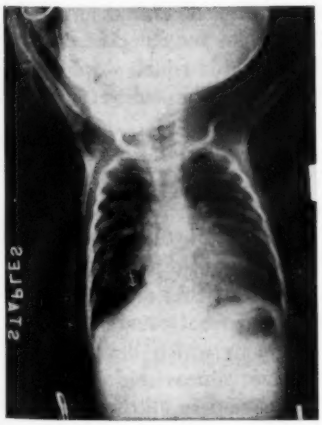

FIGURE 12 *(left)*. Early emphysema in a two month old Negro infant.

sive right heart hypertrophy accompanied, if it persists long enough, by clubbing of the fingers and toes. In the early stages, this cor pulmonale will usually react favorably to digitalis therapy.

Figure 6 shows a case of cor pulmonale with hypertrophied and dilated right heart.

As no patients were available for this clinic, I will describe one or two that are rather typical of the condition as we find it.

A 17 month old white girl was moderately well until the age of 15 months, although there had been some story of her having a few more colds than the average and not eating too well throughout her early infancy. At the time of her admission to the hospital she had, however, a dry cough with an inspiratory wheeze, anorexia with some loss of weight, and excessive sweating.

A diagnosis of asthma had been made by the referring physician. The stools seemed to be normal. Two weeks before admission she began to vomit occasionally, with paroxysmal coughing. At that time a diagnosis of suspected whooping cough was made. At the time of examination the symptoms were those of an acute pneumonic process with many inspiratory rales and wheezes throughout both lung fields, with a moderate degree of dyspnea. Her nose and throat cultures showed a growth of hemolytic staphylococcus.

Since mucoviscidosis was suspected, the duodenal juice was examined and showed no tryptic activity, but an increase in the viscosity.

Some 10 days later, an examination of the chest showed a decrease in the amount of density (figure 7). The child was discharged from the hospital on a regimen of antibiotics and pancreatic substance. However, family and medical cooperation were poor, because the referring and family physician did not believe that such a disease ever did or ever could exist.

For the next 18 months the stools remained fairly normal, and she was symptom-free, except for continuation of a dry cough and some slight sternal retraction on inspiration.

The patient was readmitted to the hospital at the age of three years. She was quite undernourished and showed rather excessive emphysema. Her stools had become bulky and foul smelling, indicating the advent of a celiac syndrome. She had been receiving penicillin aerosol inhalations at home, but her symptoms had persisted and the cough had become progressively worse.

Throughout the next year, after being hospitalized and treated, she gained 10 pounds and seemed to be progressing very satisfactorily. During this time both the family and the doctor became convinced that there was such a disease. However, six months later the infection became very much worse, and the child was readmitted to the hospital with an exacerbation of the previous findings. At this time there was extreme cyanosis with more extensive barreling of the chest (figure 8) and some enlargement of the heart toward that of a cor pulmonale. There was also some enlargement of the liver.

The nose and throat culture at this time showed *Staph. aureus* and *Pyocyanea*. These organisms were sensitive in culture to AUREOMYCIN® and streptomycin, and least sensitive to penicillin. Accordingly, the aerosol inhalations were changed from penicillin to Aureomycin and the general condition of the child seemed to improve.

Sensitivity tests of the *Proteus*-like organism later found in the nose and throat showed inhibition with Aureomycin and no inhibition at all with penicillin.

As is often the case after these children have been ill for a long time, there is a rather extensive imbalance of electrolytes. This child had a great reduction in her chlorides and an increase in carbon dioxide which would be in keeping with the loss of the sodium chloride through the perspiration.

The child died in the hospital at the age of five and a half years.

The name fibrocystic disease of the pancreas or cystic fibrosis of the pancreas or mucoviscidosis is really of no particular value as far as the etiology of this disease is concerned. We don't know what causes it. All we do is make a diagnosis which describes the condition that we see; mucoviscidosis means a thickening of the mucus in all the glands of

the body. We say that the principal difficulty was found first in the pancreas because it was thought to be the reason for all the difficulty. The absence of trypsin certainly does not have very much to do with the lung findings, but it can have something to do with the celiac problems that are present.

Another case (figure 9) was similar to the preceding one, but the child was six years old at the time of her death. Instead of there being very extensive lateral enlargement of the chest, the lung was greatly elongated and involved with fibrosis, which continued until the child had extensive clubbing of the fingers and the hands. There is an involved sibling of this child, now four years old, who gives promise of longer life expectancy because of close and continuous medical supervision plus cooperative and understanding parents.

Still another child was two weeks old at the time of admission to the hospital. She showed some evidence of atelectasis in the lower right lobe (figure 10), which made the radiologist suspect the possibility of fibrocystic disease. This was confirmed finally by a flat gelatin tolerance curve and the absence of trypsin in the duodenal juice.

At the age of two and a half months, this child developed loose, foul, watery stools and had extensive bilateral bronchopneumonic infiltration.

The infant died at the age of three months, and autopsy confirmed the diagnosis. There were cysts in the pancreas and the lungs were quite emphysematous and showed the presence of a purulent bronchitis and hemorrhagic pneumonia (figure 11).

When mucoviscidosis is suspected as a result of various clinical signs and symptoms, the diagnosis may be verified and proved by certain laboratory procedures. Of these, a determination of trypsin in the stool is the easiest to perform and is done by diluting the stool, 1:5 and 1:10, with normal saline solution and placing this mixture on undeveloped x-ray film. This is a good screening test; it is easily done and requires only a couple of hours. There is normal or increased trypsin activity, manifested by digestion of the gelatin under the spots. The absence of trypsin will be indicated by unchanged gelatin on the x-ray film. It is usually well to incubate the slide for one hour to be sure there is no tryptic activity.

This trypsin test is, however, not without some uncertainty and may indicate tryptic activity even in the presence of fibrocystic disease. Here I would like to state that not all of these patients have no trypsin at all; many of them may have a small amount and in varying degrees. I think that is the reason some of these children go on for longer periods of time without too much trouble.

The most dependable test, however, is the determination of the trypsin content of the duodenal juice by duodenal intubation under the fluoroscope. In addition, there is a rather extensive increase in the viscosity of this secretion. It has been found that trypsin may be present in the duodenal juice early in some cases and then disappear as the patient becomes worse, probably as the result of the cystic condition of the pancreas. Also, it has been suspected and found that trypsin may be present in some degree in the juice in patients with respiratory disturbances and not when the celiac syndrome and the symptoms are exaggerated.

Because of the absence of trypsin, the patient is unable to digest fat and proteins, which results in considerable loss of these substances in the stools. There may be an imbalance of electrolytes, as was mentioned before. The vitamin A content is low. There is a flat amino acid curve when the patient has been given a measured amount of gelatin and blood levels of amino acid are taken at varying intervals. If the patient is receiving pancreatic substance, the curve will be normal.

DIAGNOSIS

Trypsin-free stool
Trypsin absent in duodenal juice
Flat amino acid tolerance curve; normal when pancreatin is used
Emphysematous chest
Repeated respiratory infections
Early and persistent findings of staphylococcus in nose and throat

FIGURE 13. Recurrent atelectasis and pneumonia in a nine month old infant with temporary improvement.

Usually quite early in the history of these cases there characteristically appears a high incidence of staphylococcus in the nose and throat. Children with repeated colds should be examined for those organisms in the nose and throat and whenever they are found, the disease should be suspected. For this reason, isolation technics should be carried out in the hospital treatment of these patients so as to prevent any staphylococcal infection in other patients and the production of staphylococcal pneumonia.

A two month old Negro child (mucoviscidosis does not occur very frequently in Negroes) had a history of a dry hacking cough of one month's duration and, when seen, still had a very severe cough (figure 12). The disease was suspected because a three year old brother had the same condition. The infant's duodenal juice showed no trypsin and his stools were also negative for trypsin on two occasions. There was moderately severe emphysema and atelectasis of the upper right lobe and involvement of both hilar regions. This child died three or four months later after an increase in the involvement of the hilar region.

The last case I would like to describe was that of a three month old child who had gained less than one pound over her birth weight. Of course, she had been a difficult feeding problem and there had been numerous formula changes, all resulting in practically

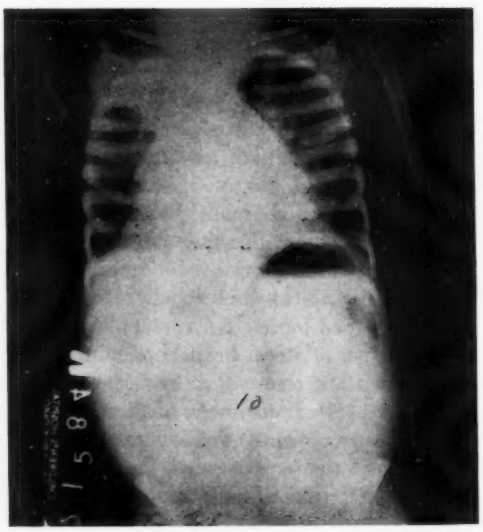

FIGURE 14. Cor pulmonale in a four year old child. There was extensive pneumonia and emphysema.

no change in the character and number of stools or in her progress. Six months later she was admitted to the hospital with a nonproductive cough, evidences of atelectasis and an extensive pneumonic process (figure 13).

She was treated for the next two or three years and, at the age of four years, she was readmitted to the hospital where she showed more of a pneumonic process with rather extensive emphysema (figure 14).

The treatment of mucoviscidosis depends

TREATMENT

Diet
Vitamin A (aqueous)
Pancreatin granules or powdered gland
Aerosol inhalations—Vaponephrine—Antibiotics—Moisture—Alevaire
Antibiotics determined by culture sensitivity
Prolonged or permanent oral use of antibiotics—penicillin, Aureomycin

on several factors. There must be proper attention to nutrition of the child in view of the large loss of protein and fat. It may be well to give these children hydrolyzed protein, but some recent work would indicate that they do better on a fairly normal diet. As a matter of fact, we are coming to find out that diabetics, nephritics, etc., do better on normal diets. Allow the child to eat practically anything that he wants.

The use of large amounts of vitamin A in aqueous form is probably beneficial. The trypsin enzyme may be partially replaced by the use of pancreatic substance either in the form of granules or of the powdered gland. It is not necessary to attempt to replace all of the gland and trypsin; a replacement of only about 10 to 20 per cent will produce very good results. It is perhaps also well to give this material directly from a teaspoon or to add it to the child's food.

A large amount of sodium chloride should be included in the diet, as much as the child can take, to replace that lost in perspiration.

The principal phase of the treatment is the use of antibiotics, preferably Aureomycin or penicillin. However, it is highly advisable that the culture obtained from the nose and throat be tested for sensitivity to the various antibiotics. It may be that in one instance one antibiotic will be better than another, and the sensitivity of the organism may change from time to time.

Aureomycin, 20 to 30 mg. per kilogram of body weight, in three or four doses in the course of 24 hours, may be used over a long period of time (three to seven years) and should be continued throughout the year, except possibly in the warmer months.

In the case of an acute infectious process in the respiratory tract, aerosol inhalations containing VAPONEPHRINE® and the antibiotic determined by the sensitivity test should be used. There is an advantage in using such things as ALEVAIRE® or Vaponephrine or moisture. Treatments may be given two to five or six times in 24 hours and will aid in dilating the bronchial tubes and in thinning and making less viscid the mucus in the bronchial tree. The treatment may be carried out in the home by means of oxygen tanks or by the use of a homemade apparatus consisting of an automobile tire pump and an ether mask to which the aerosol apparatus is attached.

Every effort should be exercised to prevent infection by helping the child avoid unnecessary exposure to colds and excess activity. He may have to cut down on his school work. Since most of these patients sooner or later develop a pyocyanic infection which does not react well to antibiotics, the problem may become more complicated. The use of acetic acid in the form of vinegar or 5 per cent solution in the aerosol may be of value.

The hope of carrying these cases over a long period of time depends on the judicious application of all of these items of treatment.

In conclusion, it may be said that because of apparent increased incidence or, at least, its more frequent recognition, mucoviscidosis constitutes a major problem in pediatrics. The essential, careful, continuous therapy requires a thorough knowledge of all facets of the disease in order to offer any hope of prolonged life for the patient and some hope and understanding for the parents.

DIAGNOSTIC CLINIC

Asthma and Asthmatoid Dyspnea

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In the treatment of patients with wheezing dyspnea it is essential to know whether true asthma is the cause. The underlying mechanisms of asthma and the principles of diagnosis and treatment are discussed.

PATIENTS with bronchial asthma are very frequently neglected. They are told that their condition is one for which nothing can be done and that if they live long enough they will outgrow it. In the meantime, they must learn to live with their asthma. The modern variant of this medical alibi is concerned largely with the psyche. Patients are told that they need only make the proper psychic adjustments to have their somas also become properly adjusted and their asthma will then disappear.

Thus, there are two very common fallacies in the management of asthmatic patients: (1) that the young patient will outgrow his asthma, and (2) that nothing can be done for the asthmatic patient whether he is young or old except to provide temporary relief.

Dyspnea

The first essential for sound management of the wheezing patient is to determine whether or not his dyspnea is the nonorganic obstructive type—in other words, whether or not he has bronchial asthma. In the differential diagnosis of dyspnea we must distinguish between two large groups: (1) nonobstructive dyspnea and (2) obstructive dyspnea.

In the nonobstructive group, functional dyspnea plays a very important role, and this type of dyspnea is frequently confused with true bronchial asthma. The so-called sighing respiration noted frequently in emotionally disturbed patients is often misinterpreted by the patient, and frequently by the physician, as bronchial asthma. The sensation of inability to aerate the lungs adequately, or the supposition that such is the case (such patients will say, "I cannot get a deep enough breath"), leads to the inaccurate belief that the dyspnea is due to asthma.

The dyspnea of simple anoxia needs little discussion. Examples of dyspnea which are not usually confused with asthma are shortness of breath at high altitudes, acute anoxia resulting from exercise, and anoxia resulting from lack of hemoglobin. Toxemic dyspnea, another manifestation of the nonobstructive

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Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

group, is infrequently confused with asthma.

More important, however, is the mechanical type of nonobstructive dyspnea which occasionally may be confused with true bronchial asthma and, in fact, under certain conditions bronchospastic factors merge with the true asthmatic picture. Examples of mechanical dyspneas are: constriction from deformity of the thorax and pressure from below the diaphragm, as from ascites or pregnancy. On one occasion years ago a patient was referred with a diagnosis of bronchial asthma, when actually the dyspnea was due to ascites resulting from cardiac insufficiency.

Lung consolidation and lung distention can both cause dyspnea. Lung distention especially is often confused with asthma. Although emphysematous dyspnea is primarily nonobstructive, a bronchospastic component frequently is involved.

Lastly, in cardiac asthma, dyspnea results from conditions other than simple oxygen lack. In this affliction, the lungs are distended by congestion. The resulting reduced distensibility, or the leather-bellows type of lung, results in the shallow breathing and paroxysmal dyspnea that we consider cardiac asthma.

The second large group of symptoms in the differential diagnosis of asthma comprises organic obstructive dyspneas. Obstructive dyspnea always must be excluded before making a diagnosis of true bronchial asthma. Several conditions may be included: (1) stenotic conditions in the upper air passages, such as tracheal webbing, anomalies, etc., which will produce stertorous breathing (such conditions are not commonly confused, however, with true bronchial asthma); (2) the wheezing dyspnea associated with foreign bodies, such as aspirated peanuts: (3) the tremendously important group of bronchogenic tumors, which apparently are becoming much more prevalent, and which are often accompanied by wheezing, coughing and dyspnea. They always must be differentiated from the wheezing of nonorganic obstructive dyspnea or true bronchial asthma.

Inflammatory diseases also may be included in the group of organic obstructive dyspneas. Such diseases lead to thickening of the bronchial mucosa or to the production of exudate without accompanying bronchospasm. And last, in the differential grouping of dyspneas, we come to nonorganic obstructive dyspnea or true bronchial asthma.

Cardiac Asthma

I am not going to say much more about cardiac asthma. I have already mentioned the reduced distensibility of the lung which leads to an exaggerated Hering-Breuer reflex. The cardiac asthmatic frequently awakens at night with acute dyspnea and goes to an open window for relief. There have been reports that injections of ADRENALIN®, given for presumed asthma, have diminished the degree of dyspnea. It is important to remember that a sudden paroxysmal attack of nocturnal dyspnea is sometimes the first sign of left ventricular failure and, under the circumstances, confusion with bronchial asthma is understandable.

Ordinarily, however, there need be no real confusion in the differentiation of bronchial asthma from true cardiac asthma. It is much more difficult to distinguish borderline degrees of developing cardiac failure in patients with asthma who also have heart disease. In them the dyspnea due to heart strain merges with the dyspnea that is attributable to true bronchospasm.

Etiology

In the etiologic classification of asthma four types are ordinarily considered: (1) typically atopic or allergic asthma, (2) asthma of infection (the so-called asthmatic bronchitis of childhood), (3) a combination of the first two types and (4) a very difficult type of asthma, sometimes called intrinsic but probably better called nonatopic and noninfective. It is this latter type which represents a very difficult problem for all of us. Its management is always difficult and its prognosis is relatively poor.

This classification was made by Dr. Harry Alexander. It is important to emphasize the distinctions made by Dr. Alexander between the two large groups of asthmatic patients. For patients in the atopic group, much can be done to prevent and relieve their asthma;

but for patients in the nonallergic, or so-called intrinsic group, treatment is largely palliative and much less effective, and the prognosis is much more ominous. The onset of atopic asthma is relatively early, with a positive skin reaction, circulating atopic antibodies in the blood which can be passively transferred and a positive family history of asthma. Complications usually are not severe, the response to treatment is generally good, and fatalities rarely occur.

But with so-called intrinsic asthma—nonallergic asthma—(I am not entirely satisfied with the term "intrinsic" because it at once presents a defeatist attitude and, furthermore, as I shall attempt to point out, often leads to diagnostic failure) the situation is different. The onset of nonallergic asthma usually is after the age of 40; attacks become progressively more and more severe; often the course is very rapid, ending in coma and death. Episodes of intractable asthma, so-called status asthmaticus, are seen more often than in atopic asthma. Complications are more frequent and include severe and progressive emphysema, which ultimately may result in cor pulmonale. A complication which is recognized with increasing frequency is periarteritis nodosa. Frequently, death terminates an episode of intractable nonallergic asthma.

What is the mechanism of the typical asthmatic paroxysm? There are three fundamental factors involved: (1) smooth muscle spasm, (2) edema of the bronchial musculature and (3) plugging of the bronchioles with tenacious secretions.

The typical atopic asthmatic paroxysm may, of course, be initiated by exposure to a specific antigen with resulting explosive antigen-antibody union. The antigen-antibody reaction results in the release of histamine, of acetylcholine and, in addition, of some other substances which have not yet been identified. We do believe that much more is involved in antigen-antibody reactions than the release of histamine and acetylcholine.

Although typical asthmatic paroxysms are produced by the stimulus resulting from antigen-antibody reactions, there are many other stimuli that are perfectly able to cause an attack of asthma. Many physical stimuli, such as result from breathing cold air, the dust caused by shaking ashes from the furnace, rapid breathing after walking briskly, are recognized as precipitating causes of typical asthmatic paroxysms. These are trigger mechanism which bring on an acute attack, but they are not etiologic causes of asthma.

Respiratory infections are major trigger mechanisms, and especially in early childhood precipitation of asthmatic attacks by infection is so important that, with surprising frequency, the young child who is developing typical atopic asthma is regarded as having asthmatic bronchitis. This error has impressed me in recent years to a greater and greater degree because, after taking the histories (I am speaking now of young children two or three years old), I have repeatedly made a preliminary diagnosis of asthmatic bronchitis or infective asthma and, after skin tests were all found negative, the assumption seemed to be confirmed. However, subsequent study of a considerable number of such children demonstrated atopic sensitivity. When blood serum from a child was taken and transferred to the skin of some nonatopic subject (usually a member of the family) and the passively sensitized sites later tested, in an astonishing number of instances passive transfer reactions to foods and inhalant factors, such as dust, dander and molds, were found. Adequately controlled positive passive transfer reactions unequivocally demonstrate that circulating antibodies are present in those children, even though direct skin reactions could not be demonstrated. We can assume very logically (and subsequent observation usually confirms the assumption) that presumed asthmatic bronchitis is, in fact, early atopic asthma. An upper respiratory infection is the mechanism that starts an asthmatic paroxysm in a child who is fundamentally atopic.

Pathologic Changes

Briefly, let us consider some of the early pathologic changes that occur in asthma. It is notable and characteristic that pathologic changes in early asthma are scant. Because the changes are evanescent and because pa-

tients with atopic asthma rarely die of the disease unless an intercurrent infection has caused death, we do not see them.

The first physiologic response in asthma is bronchoconstriction. Asthmatoid breathing can be produced in the guinea pig and in man by inhalation of histamine. However, the bronchoconstriction induced by histamine is only one phase of the allergic reaction. When a guinea pig inhales an antigenic substance, such as horse serum or egg white, to which it has been specifically sensitized, there occurs not only bronchoconstriction but, in addition, changes occur in the bronchial tree that conform closely to the changes observed in a typical asthmatic attack in man. These changes are very significant and strikingly demonstrate the difference between the chemical bronchoconstriction resulting from histamine alone and allergic bronchoconstriction due to antigen-antibody reactions. They demonstrate, furthermore, why some procedures used in therapy are helpful and why some are not helpful. I refer primarily now (and later I shall return to this point) to the use of antihistamines to counteract the histamine effect and to the use of corticosteroids in the management of intractable asthma.

During an allergic bronchospastic reaction there is not only the transitory bronchoconstriction attributable to histamine release but also eosinophilic infiltration of the bronchial wall. In guinea pigs it has been shown that after inhalation of a specific antigen, eosinophils are sequestered in the bronchial walls from 6 to 18 hours after acute shock symptoms have subsided. Accordingly, in an acute attack of asthma, both in animals and in man, eosinophilic infiltration of the bronchial wall occurs. Eosinophils are sequestered from the general circulation at the onset of an acute attack and may diminish or even disappear from the circulating blood. This eosinopenia may be attributable in part to the stimulus of stress. As the acute attack begins to subside, eosinophils are released and as they enter the circulating blood stream the eosinophil count rises very rapidly.

Epithelial proliferation of the bronchial wall occurs as an early pathologic change; there is increased formation of goblet cells and resultant increased mucoid secretion. Acute emphysema, present during an acute attack of asthma, disappears to a large extent, or completely, after the attack subsides in early atopic asthma. This reversible emphysema is quite a contrast to that often seen in the nonallergic asthma of later years, which progressively increases to irreversible emphysema with complications of cor pulmonale.

Frequently, a patchy atelectasis results from segmental plugging of the bronchial tree with mucus.

Later, in chronic asthma, thickening of the basement membrane and subepithelial layers occurs, and still later, the alveolar walls are permanently damaged and stretched so that the lungs are constantly distended, the vital capacity reduced and the breathing capacity markedly impaired.

In an acute asthmatic paroxysm there is a marked acute emphysema with temporary increase in residual air. During acute asthma attacks the complemental air and supplemental air almost disappear so that the tidal air represents the vital capacity at the moment. Expiration becomes active, aided by accessory muscles, but in spite of expiration effort more and more air is trapped in the lung, resulting in rapid accumulation of air in the residual dead space.

Principles of Treatment

Fundamental principles in the management of asthma are: (1) The recognition and avoidance of specific inhalants. (2) Hyposensitization with those things that cannot be avoided. (Hyposensitization actually induces immunity. We believe that the so-called blocking substance that is developed by adequate immunization is probably a univalent antibody.) (3) Prevention and control of respiratory infections by the judicious use of antibiotics. (Sensitization by indiscriminate use of penicillin and other antibiotic or chemotherapeutic drugs must be avoided. Such drugs should be administered only when there is specific indication for use. They should not be used for simple coryza.) (4) Palliative measures to bring about immediate relief.

In the palliative management of asthma there must first be an endeavor to eliminate or reduce known or suspected specific antigens. Second, induce bronchial relaxation by epinephrine, by any one of the sympathomimetic drugs or by the use of intravenous aminophylline.

Third, clear the bronchial tree of tenacious secretions by means of iodide or ammonium chloride to liquefy the secretions. It is astonishing that both in hospital clinics and in the private practices of many physicians, patients go on and on without iodide medication in spite of the widespread recognition of its importance. Frequently persistent asthma is relieved as soon as iodide medication is prescribed. Be sure, however, that iodide can be tolerated by the patient.

Fourth, apprehension must be relieved. It is important that sedation is not carried to the point of excess where the patient can no longer raise sputum and cannot help himself expel the occluding mucus from the bronchial tree. Fifth and last, any infection present must be controlled.

Everyone who talks about asthma warns of the dangers of prescribing morphine to patients with asthma. Morphine and similar drugs are depressants of the respiratory center. If a marked degree of emphysema has developed, depression of the respiratory center results in increased retention of carbon dioxide, so that not infrequently carbon dioxide narcosis, coma and ultimate death have followed the use of morphine derivatives.

Hyde Salter's remarks about morphine in his classic treatise, published in 1868, emphasized the hazard of using opium in the treatment of asthma.

Oxygen tends to dry the secretions and so may increase rather than relieve wheezing. Oxygen should be used when there is cyanosis but it is not helpful in the routine management of asthma.

I will mention briefly the very important role of corticosteroids in the management of intractable asthma. I referred previously to the infiltration of the bronchial musculature with eosinophil cells, which is in fact an inflammatory response. One major role of corticosteroids is the inhibition of inflammatory responses. For example, although corticosteroids do not inhibit atopic or histamine wheals, they will prevent or obliterate the inflammatory reaction which occurs in a positive tuberculin type of reaction. Similarly, corticosteroids will eliminate the inflammatory infiltration of the bronchi which occurs during an acute paroxysm of asthma and thus help to bring the attack to an end. Corticosteroids do not cure asthma; they do not alter underlying sensitivities; they do not prevent antigen-antibody union; but corticosteroids are invaluable as palliative aids in the management of asthmatic patients when ordinary measures will no longer bring about relief.

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DIAGNOSTIC CLINIC

Rehabilitation of The Hemiplegic

HOWARD A. RUSK*

New York University College of Medicine, New York

Unfortunately, in the past, the medical attitude toward hemiplegia has been one of hopelessness and helplessness. If a dynamic approach is used, however, the hemiplegic is not a lost cause. Spot checks have shown that 90 per cent can be taught ambulation, self-care and urinary and fetal continence, and 40 per cent can be taught to do gainful work.

HOWARD A. RUSK

To a degree, rehabilitation of the hemiplegic involves almost every physician, because most physicians have hemiplegic patients—patients who are hidden away some place, in back beds of wards, in back bedrooms or in attic rooms in homes, or who are being maintained in county institutions.

Before I discuss hemiplegia, I would like to take up another problem that, unfortunately, every doctor meets from time to time, and that is the immediate management of the traumatic paraplegic and quadriplegic patient. I am sorry to say that when these patients are sent to us for training to live the best lives they can with what they have left, it takes us twice as long to clear up the complications due to improper management as it does to train the patient. Those complications are bed sores, contractures and kidney complications, practically all of which could be avoided if the patient were approached properly from the moment he is seen.

Some of the most tragic people that I have ever seen in my experience in rehabilitation have been individuals who have not had proper initial care. I think of one who illustrates the group, a young Navy flyer who crashed his plane and was able to walk a hundred yards before the plane exploded and burned. He was on the ground when the aid men picked him up, had sensation and was able to move his lower extremities, but because the book said to carry these patients in hyperextension, they forced him into hyperextension. Now he tells tragically of his trip to the hospital during which his legs went to sleep. For by the time he arrived there 20 minutes later he was a paraplegic with a transected

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cord. Such patients should be carried in the neutral position on a firm object of some kind; the simplest one is a door. You can always take a door off its hinges, slide your patient gently onto it in the neutral position, and keep him on the door until after the x-rays are taken. Then you know the deformity and how to handle it.

Remember that in the first six weeks after injury the patient is most prone to the development of decubitus ulcers, that there is a very marked disturbance of protein metabolism, and that, in the younger group, the disturbance is much more violent and vicious than in the older group because of all of the accentuated endocrine mechanisms. These patients have to have protein in the early days of treatment, they have to have careful nursing, they have to have protection from pressure. Otherwise, there will be terrific decubitus ulcers which will be very difficult to manage. If ulcers develop, the best treatment, in our experience, in addition to good nursing and the removal of pressure, is the use of dried plasma, either with or without balsam of Peru, packed into the wound and used as a dressing, with or without impregnation of gauze. If there is undermining, gauze must be used. A preliminary report on our first series of cases was published in the November 1953 issue of the *Journal of the American Medical Association*.

We are convinced that there is a proteolytic enzyme in plasma that helps to clean up the slough as well as to promote healing.

As far as urinary function is concerned, we prefer to use either tidal drainage or a retention catheter until the period of shock is past, and then initiate a regimen of bladder training.

It is of utmost importance—and I stress this again—to keep up the patient's general nutrition.

One other factor about which I would like to urge caution is illustrated by a case I saw in rounds recently. The patient was a young man with a traumatic paraplegia, who had been well handled; he had had early laminectomy—we believe in early laminectomy for thoracic and lumbar lesions (we believe it is wiser to wait with cervical lesions)—but when the surgeon walked out of the operating room and came to see this young man in his room he said, "I want to tell you that your spinal cord is transected and you will never walk again." When a man is in the shock of such an extremely traumatic incident as paraplegia, he must have a little time to live with his disability, to learn to know it and to take it gradually. In a booklet prepared for paraplegic veterans, we said, "You have a paraplegia. Up to now there is no way that science knows to heal a cord so that it will function. Many years ago, or a few years ago, there was no treatment for diabetes or pernicious anemia and now it can be simply handled. The job now is up to you. We can teach you to walk on braces and crutches and to live a full life."

Eighteen hundred of the original 2500 veteran paraplegics in World War II today are living in their own homes, driving their own automobiles, and 80 per cent of that group are either in schools or in jobs.

"We are going to give you every chance to see what will come back and we will protect or back you indefinitely if there are signs of return." By indefinitely, I mean months; but allow the patient to live with his disability and to come to it gradually, and you will save that individual a great deal of very acute suffering.

Unfortunately, in the quadriplegics, 80 per cent of the transections occur between the fifth and sixth cervical vertabrae—a bad place because it catches the triceps and all or part of the finger flexors, and if the patient can't push he can't crutch walk. But even with these individuals, don't present too gloomy an outlook as to life, because we have worked with many persons with complete transections between the fifth and sixth cervical vertebrae who are earning their own living, who are in school, and who are living a reasonably good life of sorts. I emphasize this because, as I have stated, we see the end results of some of these preventable tragedies.

Hemiplegia

There are estimated to be 1,500,000 hemi-

plegics in the United States, a figure which is gradually but steadily increasing. This is a situation that we in medicine have created. We have caused this incidence of hemiplegia; we have caused it by better surgical technics, by knowledge of nutrition, by antibiotics, by everything that has gone into making medical care what it is today and that has increased life expectancy from 49 years in 1900 to 68 years today. There are 12,000,000 people in the United States today beyond the age of 65. A man of 65 today has an expectancy of 14 years and a woman of 17 years. This is the age at which hemiplegia is prevalent. In the past we have had a more or less defeatist attitude about this situation. "Poor old Joe has had a stroke; he is on the shelf." We have forgotten that Pasteur did some of his greatest work after his hemiplegia, and, if the recent newspaper reports are correct, Winston Churchill is apparently doing quite well after recovering from what was reported to be a cerebral accident. We recently analyzed our own program which covers 1000 patients who have had apoplectic strokes. The average age of the patients was 63. Most of them were typical Bellevue Hospital patients who had been incapacitated by their strokes from periods ranging from three weeks to 21 years, an average of nine months. With a proper training period, that lasted an average of seven weeks, 900 of these patients were able to walk and to meet the needs of daily living; 400 went back to some type of work.

We know that 90 per cent of all strokes are due to vascular occlusions. The other 10 per cent are caused by hemorrhage, emboli and various other factors. I want to stress the management of the simple "garden variety" of stroke.

We believe in early ambulation. We like to get a patient's feet over the side of his bed within 48 hours after he becomes conscious. If the patient's stroke affected his right side (as 40 per cent of them do), you know that there will be aphasia of some degree, either temporary or permanent. The first thing to do when the patient becomes conscious (and this sounds so simple that possibly I shouldn't say it, but, again, I say it because I have seen what happens when we forget sometimes) is to sit by the side of the bed, take the patient's hand and say, "You have aphasia. I know what it must mean because I know how irritated I become when I can't remember somebody's name, and I have some idea how you must feel when it is multiplied by infinity. I know that you haven't lost your mind, I know that you know what I am saying to you. There is a way that you can be trained to speak again, to communicate, and we are going to start a program as soon as you are able." Tell the family the same thing. I have seen patients who have gone for months thinking that they had lost their minds, that the mental institution was the next place, simply because someone had forgotten to say these simple things.

If your patient has malignant hypertension, a training program, other than one of the simplest type, is not feasible because the life expectancy is too short. You teach him the simple things that he can do to help in his needs of daily living and self-care, and you don't try to go much beyond that.

Patients with such brain damage that they cannot remember tomorrow what they are taught today are not feasible for training because you can't carry water from the well in a sieve. Patients with some severe cardiac damage in whom the added physical strain of training will overload their limited cardiac capacities are not feasible for training. We feel all others are.

In cases of hemorrhage, early ambulation means in about four to six weeks, because usually the patient is so profoundly hit that it takes that long before you can get to him to train, and, as you know, the mortality rate in hemorrhage is more than 80 per cent.

In cases of embolic phenomena you have to be guided by your training program and by the general systemic situation. If it requires rest to try to prevent a second embolus, then rest must be given, but otherwise, as I have said, we believe in early training.

Before the patient becomes conscious there are a number of things you can do that will save you a lot of trouble, and they are all very simple. In the first place, you put sandbags on the outside of the patient's affected leg to

prevent external rotation; you put a small pillow in the axilla and a sandbag on the outside of the upper arm to prevent external rotation of the shoulder. The first day, if you have a physical therapist, it is simple; if you have a nurse, it is relatively simple because it is so easy to teach; if you have an intelligent family, it is still simple if you will teach them to take the joints on the affected side through a full range of motion 10 times four times a day. If that is done, the patient will not get frozen shoulders, and he will not have to go through a long, painful and really unnecessary period of coming back.

When the patient is able to drop his feet over the side of the bed, you hold him in that position. If it has been only a few days since his stroke, you will have no problem; if it has been weeks, the patient will become faint and have the so-called "convalescent shakes." Everybody is familiar with it, and it is due to the fact that the individual has to adjust to a new hemodynamic situation as far as the brain is concerned. You watch the patient, and when his color begins to change, you put him flat. The next time you sit him up it will be for half a minute longer, and within a relatively short period of time, he can be up a matter of hours.

As soon as the patient has been sitting a few times and is stabilized, you have him stand up by the side of the bed; there are certain reasons for this, especially in older people. Bed is their harbor; it is the thing that they are familiar with and that they tie to, and if you start their early training around the bed, you will relieve a lot of anxiety in your older and sometimes slightly disturbed patients.

You cannot evaluate absolutely what you can do trainingwise until after an eight week period, because, as you remember, edema is present for from six to eight weeks while the lesion is healing. We have seen patients become anxious to the point of frenzy, because we took them around the corner into the gymnasium before we started them at the bedside. I think you will find that simple suggestion helpful with your older patients.

We don't allow walkers in our hospital, because if you have seen and studied the gaits of patients in walkers or have walked in a walker, you know that you have to walk with your hands fixed to your side. Try to walk around a block twice with your hands tight at your sides, and you will find that you can't do it unless you consciously try, and even then it is very clumsy and uncomfortable. These patients have to learn to walk a reciprocal gait, just as you walk, subconsciously, and that pattern has to be brought back if the patient is going to walk well. The simplest way to do that is with a set of parallel bars, not fancy parallel bars like those in a gymnasium, but a pair of parallel bars of a height that you can grasp easily. The bars can be made by a plumber of simple one inch pipe, so that the patient in the bars can start and balance, turn and catch, and regain his balance. If one side of the patient is affected to the point that he has no function in his hand, put a glove on his hand, fasten it with a pin or adhesive so that the paralyzed hand can slip along on the bar, and again he can learn reciprocal gait.

As soon as we get to this stage of the game, we use a very simple device called pulley therapy. You have to have a five cent window pulley and about 25 cents worth of clothesline rope. You put a hook in the door sill or on a curved piece of pipe over the foot of the bed. Next, put a webbing around the patient's hand, one around the wrist and one around the palm, with rings like those used on the old-fashioned tables to get patients in the lithotomy position. Then, place the patient in a chair under the pulley and he can exercise his own affected side. You get a double play on that. In the first place, he will do twice as much the first day as he would allow you or a member of the family or a therapist to do, because he knows his own pain threshold. Secondly, you are strengthening the arm that the patient will need for balance and for a cane and for his whole walking program. By changing the angle of the chair, you can provide any motion of the shoulder that you want, and it can all be done very simply.

When you start your patient in gait training in the bars, be sure that you don't allow

him to circumduct and get in a pattern which you have seen many times. There is a real reason for it. I take it for granted, of course, that there is a footboard at the foot of the bed to keep the pressure of the covers from increasing the foot drop. If the illness is protracted, you make a little half-shell cast, a night cast, for the patient that will keep the foot up at a right angle. If you test your patient and ask him to bring up his toe, in a large percentage of cases he is unable to do it, but if you will have that patient stand at the side of the bed and flex his knee, you will find that the toe comes up automatically. That is the climbing reflex—one of the most primitive reflexes and the first to come back automatically in the lower extremity.

Utilize what nature has provided and teach your patient to walk at first with an exaggerated bend of the knee. His ankle will flex, but the problem will be that, when the patient comes up in this position and flexes and comes down, he is unstable and that is when fibular fractures occur if something isn't done to prevent them. Give the patient a little double-bar, short-leg brace that comes up to the midcalf with a 90 degree stop, fastened to the heel of his shoe in the anatomic position, so that when he walks his toe comes up and when he comes down he is solid. More than 60 per cent of our patients require a simple short-leg brace. The brace will help tremendously to control clonus in the spastic hemiplegic, because, as you remember, 90 per cent of the clonus originates in the toes. With a 90 degree angle, or a few more degrees if you need it, the patient hits the ball of his foot, keeps the weight off his toes, and loses a great percentage of the clonic impulses that come from the toes.

If your patient doesn't have to be braced and has a clonus, take a quarter-inch piece of leather, or, if you want to try him first, a quarter-inch piece of wood, an inch wide (just the width of the sole), fasten it with adhesive and let the patient walk with that for a few days. This will control much of the clonus.

I want to tell you about one interesting group of patients and what some of them can do. There is a simple way to set up a kitchen at home that can be run entirely with one hand. We have scoured the market and have delineated where to get this material. There are one-handed rolling pins. If you want to peel a potato with one hand, you can do it very simply. Take a board, put four little suction cups on the bottom of it and drive a nail through the middle. Push the board down so it is solid; put a potato or carrot on the nail, and peel it with one hand. There are now, I guess, at least 100 hemiplegic women who run their homes and do all their work. But most interesting are the hemiplegic men, whom with fear and trembling I approached some three years ago. We had a couple in their houses at the same time who obviously could not go back to their jobs. There was a real situation at home; the wife was able to work and wanted to work, and those men had to keep their dignity. As I say, with fear and trembling, I approached them and asked how they would like to learn to do housework, thinking I might get thrown out on my ear. They are the most grateful group I think we have ever trained. They were enthusiastic in their training. They learned to cook and to wash dishes and to do all of these things. They and their wives arranged their little kitchens. The wives continued to work, the husbands took care of the homes and of themselves. They maintained their dignity and the families remained on a happy, even keel.

We have not been disheartened in our management of the hemiplegic. We have been gratified with the results that can be had with just a modicum of training. Ninety per cent of these patients can be handled in your own practices by following very simple rules.

My staff and I have prepared a monograph that is available to any interested physician.*

In the past we have always thought that a patient who had had one stroke just waited until he had the second or the third and died. A recent analysis has shown that a patient beyond the age of 65 who has a stroke and who survives for eight weeks is no more or less likely to have a second stroke than any-

*Requests should be sent to Dr. Howard A. Rusk, New York University College of Medicine, New York City.

one else in his age group. I think that may be very comforting to some of your older patients, because this fear has hung over them like the sword of Damocles.

One other point I might add is that we have found it helpful to use small doses of cortisone for difficult patients. If the patient who has had a stroke is very unstable emotionally, cries all the time and has a sore shoulder is given 50 mg. of cortisone for the first four or five days and then maintained on a dose of 25 mg. (we have been able to maintain some on 12.5 mg.), the mild euphoria they obtain stimulates them to train. The cortisone removes some of the spasticity and a lot of the pain. We had one patient who had had two strokes, a fractured hip that had been pinned and a fractured back from osteoporosis, who was a sniveling piece of protoplasm, unhappy and crying all the time, who has been carried almost two years on a very small maintenance dose daily. He is now walking steps, goes out in a car, and has a life of sorts.

We have never had any problem as far as increased blood pressure is concerned. When you have patients with hypertension in a training program where they feel that they are doing something that will help them get back into life again, their blood pressures will be from 10 to 20 points lower than they are when they sit in bed and worry about themselves.

In our group of 1000 patients we have had only two recurrent cerebral accidents in the entire series, and they both happened at night.

I have briefly described our experience with the simple management of a difficult problem with the hope that you will find it helpful in one of medicine's No. 1 problems.

Postgraduate Clinical NOTES

18. THE FACE IN DIAGNOSIS. III.

The contour of the face in certain conditions permits of instant diagnosis. An example is seen in acrocephaly, the achondroplasic, the mongol; the rare condition of oxycephaly and hydrocephaly need be seen only once to be immediately diagnosed. In osteitis deformans the prominent forehead attracts attention. In leontiasis ossea the bones of the cranium and face are asymmetrically enlarged; the superior maxilla is particularly prominent. An opportunity to recognize leprosy is not likely to present itself to many physicians in this country; the leonine facies is due to the bronzed and coloured patches that form the cutaneous creases and ridges. The virile facies displayed by a woman suffering from a tumour of the suprarenal cortex or of the basophilic cells of the pituitary hardly requires description.

Pierrhos StKatsareas, *Lancet*, October 31, 1953, p. 929

SCIENTIFIC EXHIBIT

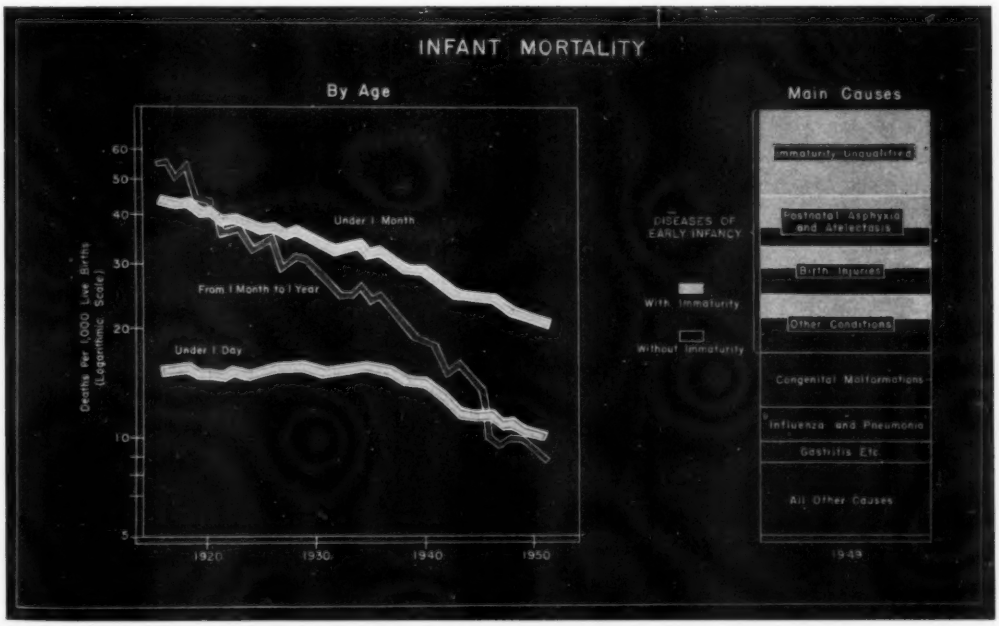
Emergency Examinations of the Newborn

GEORGE COOPER, JR.

University of Virginia Hospital, University, Virginia

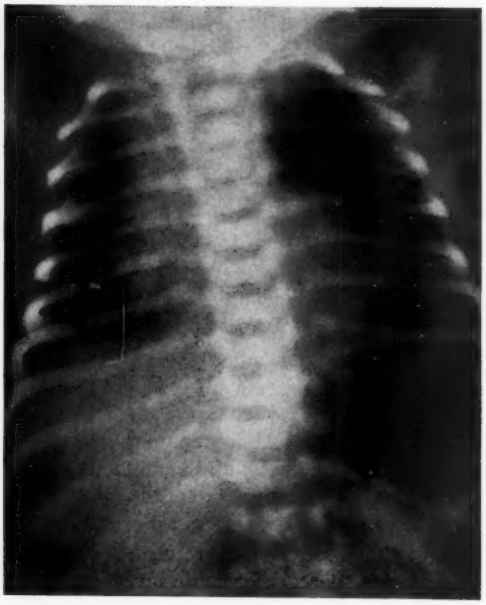
BECAUSE infant mortality rates in the first day and first month of life are not declining nearly as rapidly as in the second to twelfth months, great emphasis should be placed on any possibility for reduction of mortality in the newborn.

Prematurity and uncorrectable congenital abnormalities will always be great obstacles. Still, successful treatment in this age group depends to an unusual degree on quick action, and the roentgenologist often can make vitally important contributions to the solution of emergency problems in the newborn. The purpose of this exhibit is, therefore, to illustrate how prompt roentgenographic investigation of certain symptoms can save lives.



RESPIRATORY EMBARRASSMENT

Respiratory embarrassment in the newborn can be caused by any one of several conditions. In some cases accurate diagnosis and correct treatment make the difference between life and death. Roentgenographic assistance should be sought promptly and regularly.



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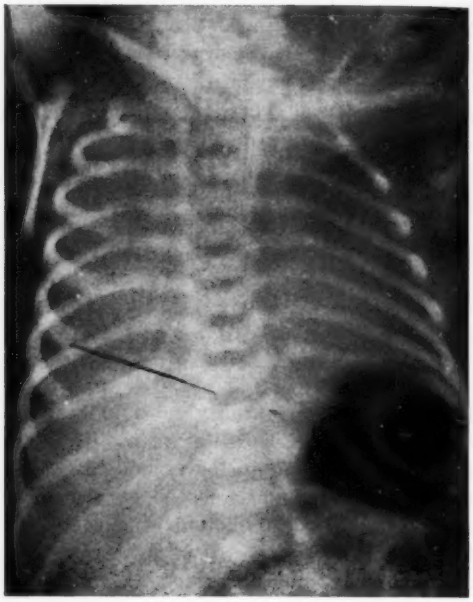

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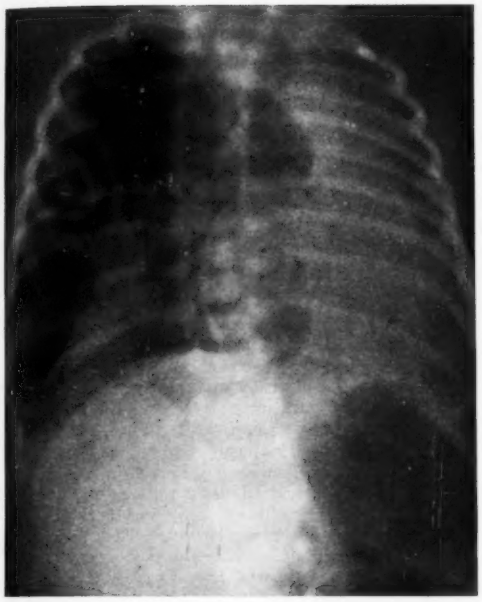
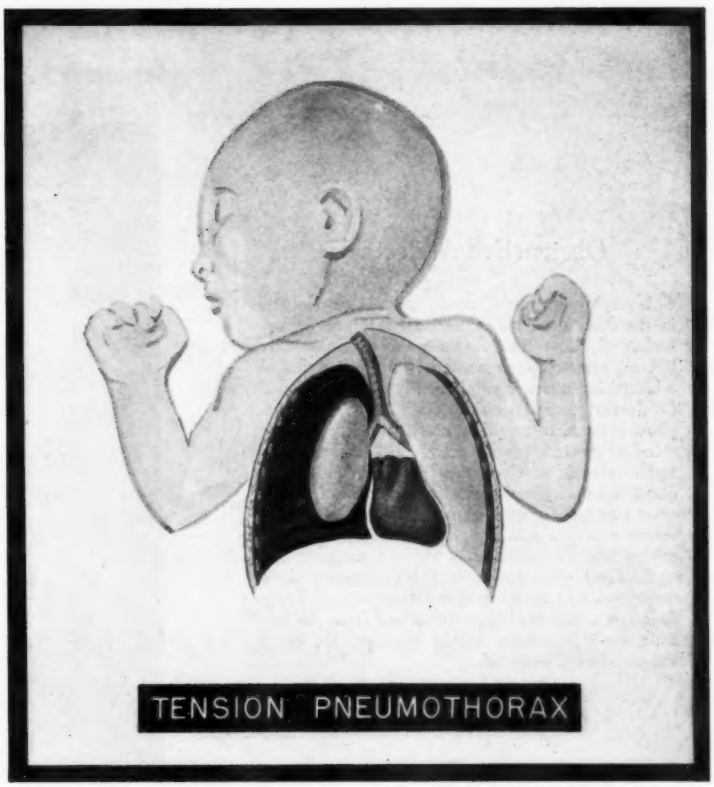
Pulmonary Hyaline Membrane Syndrome

To illustrate what can be accomplished, consider the chest roentgenograms of an infant with pulmonary hyaline membranes. Severe cyanosis and clinical manifestations of asphyxia appeared during the first day of life, yet roentgen examination demonstrated good pulmonary aeration. The finding of this unique combination, peculiar to the early stage of the pulmonary hyaline membrane syndrome, led to correct treatment and, in five days, to a well baby. The infant was left strictly alone in an atmosphere of increased oxygen concentration and mist; it was not fed and it received antibiotics. The baby manifested the usual remarkable course of infants who survive this condition. The cyanosis and asphyxia were gradually relieved while serial chest roentgenograms demonstrated progressive clouding. Both clinical and roentgen abnormalities had disappeared by the fifth day, and the baby is now a normally developed child. If roentgen assistance had not been sought when clinical symptoms first appeared, the correct diagnosis might not have been reached until too late. If bronchoscopy had been attempted, the already severely embarrassed baby might easily have died. If it had been fed, since infants with this condition regurgitate easily, aspiration might well have tipped the scales the wrong way.



Tension Pneumothorax

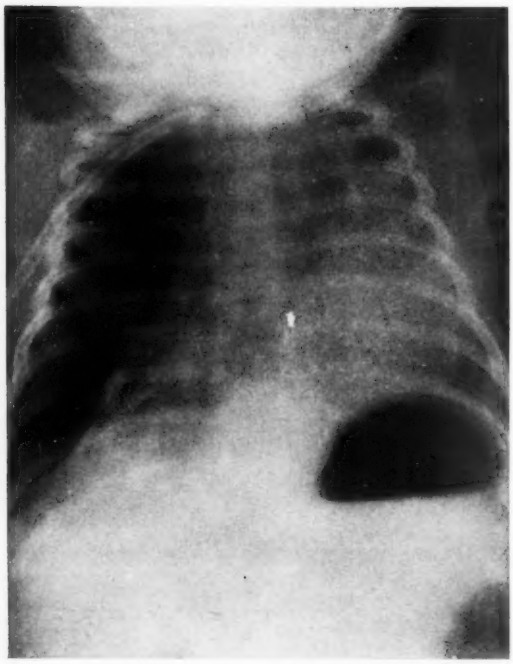
Respiratory embarrassment may be caused by a tension pneumothorax. In the case illustrated, roentgen assistance was not sought when symptoms first appeared; diagnosis and treatment were deferred, and the baby almost died. Cyanosis and dyspnea appeared during the first day of life and became progressively more severe, but the baby was not referred to our Outpatient Department until the fifth day of life. It arrived in a moribund condition, and was rushed to the X-ray Department where a roentgenogram clarified the situation. Immediate establishment of closed drainage saved a rapidly waning life.



SYMPTOMS:
Progressive respiratory and circulatory embarrassment; referred on fifth day in moribund condition

X-RAY:
On admission

RESULT:
Closed drainage saved child's life

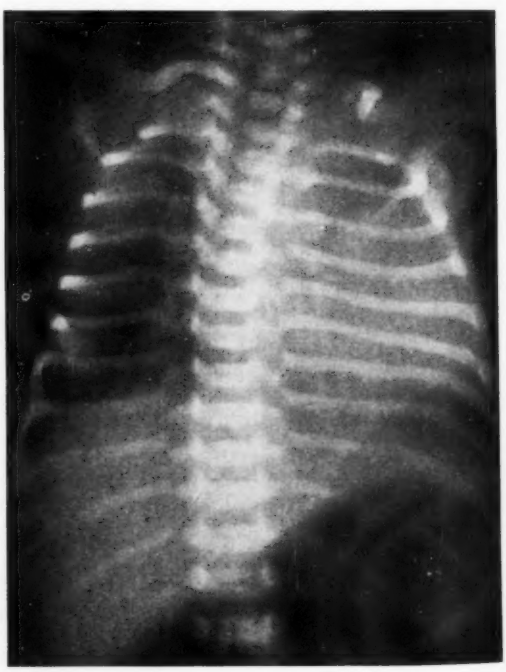


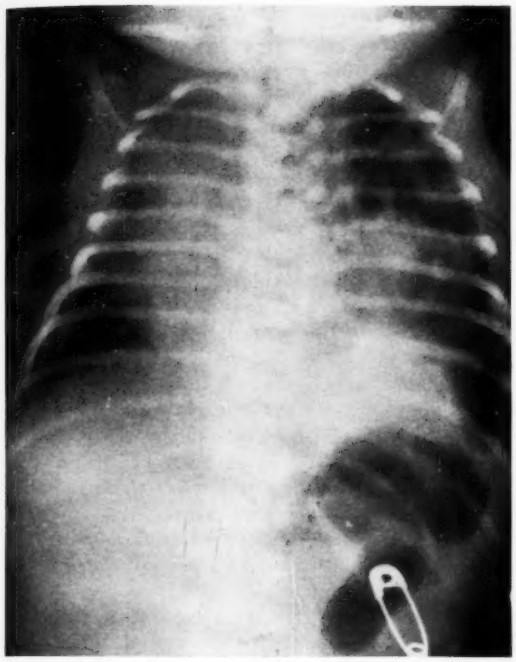
Congenital Cystic Disease with Bronchopleural Fistulas

The illustrative case emphasizes the success with which the thoracic surgeon can perform lobectomies in the very young. The roentgenogram is the admission study of a 4 week old baby who had suffered from progressive dyspnea since birth. It, too, was referred in a moribund condition. Immediate roentgen examination demonstrated a tension pneumothorax and pulmonary cysts in the partly collapsed lung, making it evident that one or more cysts had ruptured through the visceral pleura. An emergency thoracotomy was performed; a cystic right lower lobe was resected, and the infant recovered nicely. The close call with death was unnecessary. The diagnosis should have been established by roentgen examination as soon as the dyspnea was noted. Successful lobectomies have been performed repeatedly in infants less than 2 weeks old.

Obstructive Atelectasis

A varying amount of nonaeration is physiologic in the first few days of normal, full-term babies and in the first four to six weeks of premature babies, but atelectasis secondary to obstruction of a bronchial lumen is emphatically not physiologic. Clinical differentiation is vital because incomplete expansion requires no treatment but the relief of obstructive atelectasis by bronchoscopy and suction is an emergency procedure which reduces morbidity and mortality. The infant whose chest roentgenogram is shown suddenly developed severe cyanosis and dyspnea during the second day of life. The collapse of the left lung and the mediastinal shift shown in the emergency chest roentgenogram established the diagnosis. At bronchoscopy a mucous plug was sucked from the left main stem bronchus. Within minutes, the child was completely relieved.





Diaphragmatic Hernia

Usually thoracic gas shadows arranged in an intestinal pattern make the roentgen diagnosis of diaphragmatic hernia obvious. Occasionally, a small amount of opaque oil will have to be followed through the gastrointestinal tract. Unless corrected promptly by reduction of the hernia and surgical repair of the diaphragmatic defect, this condition may cause sudden death due to visceral dislocation and intestinal obstruction with consequent vomiting and aspiration pneumonia. If the infant survives and longer delay is permitted, surgical repair becomes difficult because of underdevelopment of the abdominal cavity.

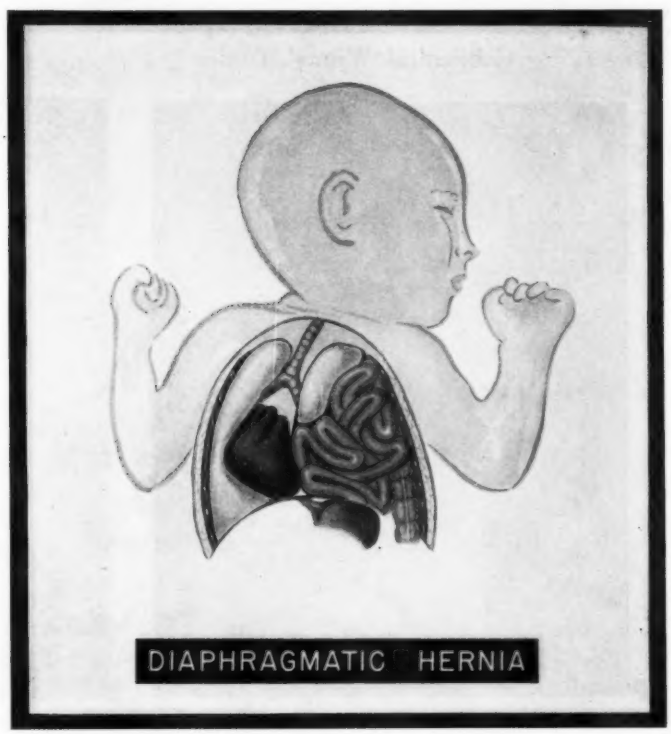
The case selected for illustration received ideal handling. Respiratory embarrassment plus physical signs of mediastinal shift led to roentgen examination at eight hours after birth. Surgical repair was performed at once, and at 48 hours the infant was nursing.

SYMPTOMS:
Respiratory distress

PHYSICAL SIGN:
Mediastinal shift

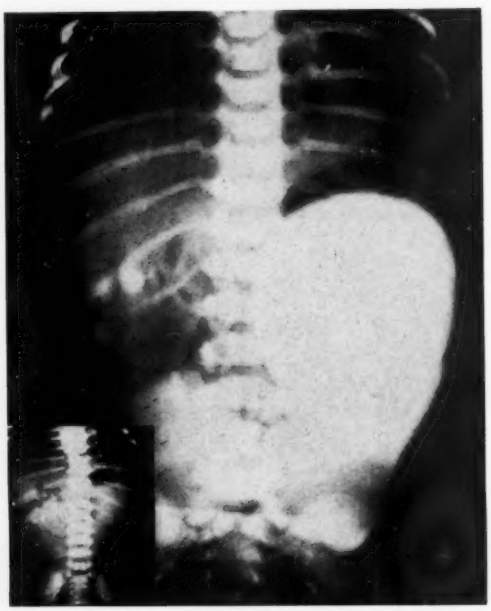
X-RAY:
At 8 hours

RESULT:
Immediate surgical repair; baby nursing at 48 hours

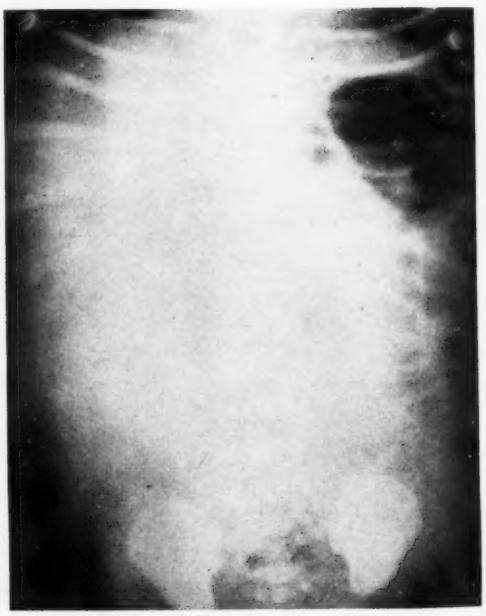


Congenital Wilms' Tumor

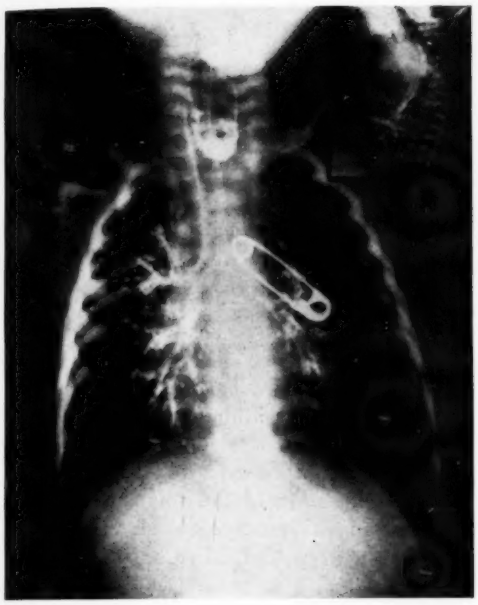
The finding of an abdominal mass other than an enlarged liver or spleen is an emergency calling for immediate investigation, including roentgenographic examination. A number of conditions may be responsible, but only rarely is one found in which prompt diagnosis and treatment do not result in reduced morbidity and mortality. In each of the three cases illustrated, an abdominal mass was discovered at birth. With roentgen assistance, it was possible to proceed with surgery within 48 hours. All three infants are now developing normally and are 3 years of age or older.



Congenital Hydronephrosis



Congenital Ovarian Cyst



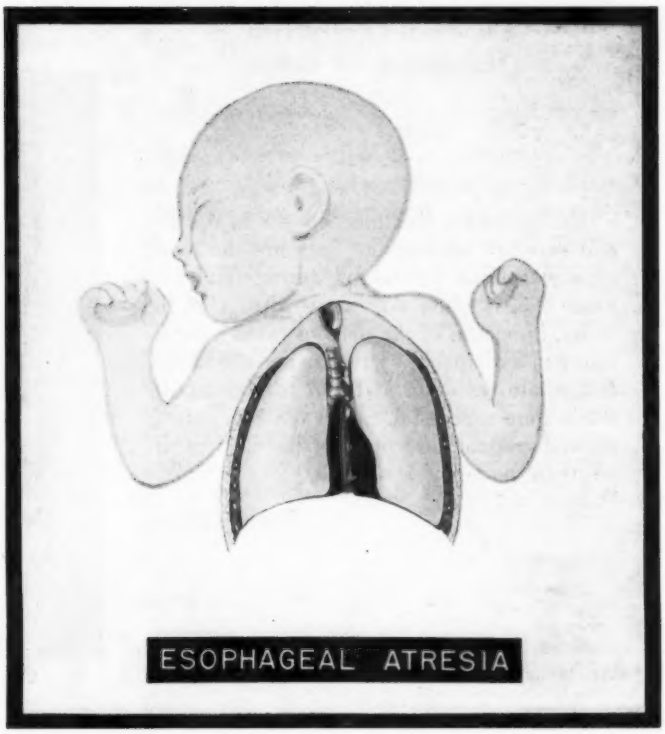
Esophageal Atresia

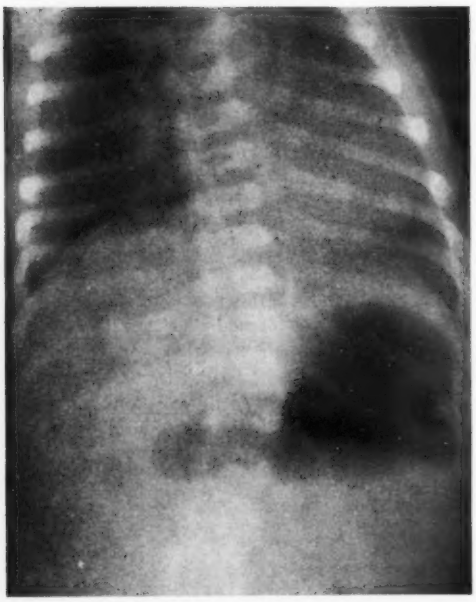
If abnormal drooling is not noted before the first feeding, regurgitation of this feeding should lead to prompt action. Esophageal atresia, with or without tracheal communication, is usually the cause. The condition is an emergency of the first order. Pneumonitis and atelectasis due to aspiration of saliva and food may develop in the first 24 hours of life. In the case shown, the roentgen examination was performed 20 hours after birth and immediately after regurgitation of the first feeding. Immediate surgery was followed by excellent recovery. Abnormal drooling had been noted before the feeding. Ideally, the roentgen examination and surgery should have preceded the feeding.

SYMPTOMS:
Drooling from birth; regurgitation and cyanosis with feeding

X-RAY:
At 20 hours

RESULT:
Immediate surgical correction—excellent recovery





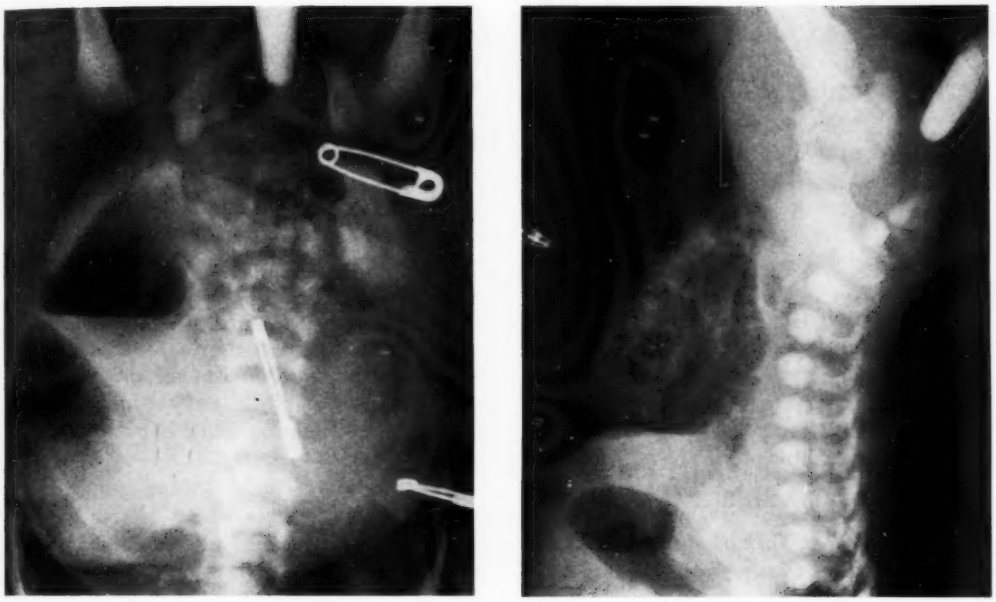
Duodenal Obstruction
(Malrotation of Colon)

The usual cause of vomiting and distention in the newborn is obstruction of the small bowel or upper colon. Surgical correction is often lifesaving. Time is of the essence. Roentgen examination of the abdomen should be carried out as soon as a suspicion of obstruction arises. Though the exact cause may not be determined preoperatively, it is not often that its level cannot be accurately located by the demonstration of distention proximal to the obstruction and collapse distally.

Roentgen examination did not reveal the cause of the demonstrated duodenal obstruction, which was a constricting band associated with a malrotation of the colon. But it provided sufficient information to lead to immediate surgery—and a live baby.

The peritoneal calcium deposits in the second case are interesting. They are the result of a meconium peritonitis during fetal life. Since this is often due to an atresia of the ileum, the cause of the demonstrated obstruction was anticipated by the roentgen findings. Immediate resection and end to end anastomosis were successful. Serial roentgenograms showed gradual absorption of the calcium deposits in the next few months.

Meconium Peritonitis
Atresia Ileum



Imperforate Anus with High Atresia Rectum

Uncorrected obstruction of the lower bowel will also produce vomiting and distention. But lower bowel obstruction should be recognized and corrected before this clinical picture develops. An obvious but frequently overlooked indication for abdominal roentgenographic examination of the newborn is failure to pass meconium or scanty passage. The finding by digital rectal examination of a perforate anus does not remove the necessity of making certain that normal elimination of meconium takes place within a few hours after delivery. Complete atresia or stenosis of varying degree may occur above the examining finger. The level of the obstruction can usually be determined by roentgen examination. Even when the anus is imperforate, useful preoperative information can be obtained by taking roentgenograms with an opaque marker on the anal dimple while the baby is inverted. If the blind rectal pouch is not filled with meconium, gas rises to distend it, permitting accurate measurement of the distance between skin and pouch. Sometimes, as in the case illustrated, a perianal approach by the surgeon is impossible and might lead to a fatality. The infant shown has a colostomy and is developing nicely.

CONCLUSIONS

Close cooperation between pediatrician and roentgenologist leads to quick and often life-saving solutions of emergency problems in the newborn. As illustrated, prompt, accurate diagnosis and prompt, skillful treatment reduce morbidity and mortality.

Pediatrics IN GENERAL PRACTICE

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Nephrosis in Children

HENRY L. BARNETT AND
MADOKA SHIBUYA*

The New York Hospital-Cornell Medical Center, New York City

MANY parents of children who develop nephrosis either have never heard of the disease or have not known that it occurs in children. At the present time, the physician treating a child with nephrosis is confronted with the task of telling such parents, in some way, the following facts:

(1) The cause of nephrosis is not known. This means that *specific* treatment of the disease is not possible. It means also that, to our knowledge, nothing the parents did or failed to do could have prevented the disease. Finally, it explains in part the many differences of opinion between specialists in the field concerning treatment and prognosis.

(2) At present, it appears that about one-half of the children with nephrosis recover. However, the final outcome of the disease in an individual child, which is what the parents want to know, cannot be predicted.

(3) The duration of the disease varies but is usually discouragingly long. In the group of children who recover, the active disease commonly lasts between one and three years. In the group of children who do not recover, death from renal insufficiency usually occurs in the absence of nonrenal complications within a similar period, although some of the children survive for many years.

The parents of a child with nephrosis must eventually know these and many other facts about the disease. Once their child has nephrosis they will be confronted with conflicting opinions about many aspects of the disease which will confuse them. Because of the chronicity of the disease and especially because of the forbidding uncertainty of the outcome, they need great support from the physician. To supply this help the physician needs to be certain of what is and is not known currently about a disease which, though it is being

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actively investigated in a few medical centers, he himself sees infrequently.

Definition

At the present time, nephrosis cannot be classified etiologically within the group of so-called medical diseases of the kidney. Consequently, the only clinical value of any classification would be if it provided a basis for predicting the natural course of the disease and the final outcome. Thus far it has *not* been possible, on the basis of any clinical or laboratory examinations, to differentiate early in the course of the disease between the children with nephrosis who will recover and those who will die of renal insufficiency. Until more is known, therefore, concerning causes and mechanisms in this disease the most adequate working definition appears to be as follows:

The term *nephrosis*, as used here, designates clinically the disease which: (1) usually begins insidiously in young children with the onset of edema associated with proteinuria, hypoproteinemia, hypoalbuminemia and hyperlipemia; (2) is not preceded by any evidence of acute glomerulonephritis; (3) *may or may not be accompanied by transient or persistent hematuria, hypertension or reduced kidney function*, and (4) may result in complete recovery or in death from renal insufficiency.[a]

Clinical Considerations

In following a large group of children with nephrosis several more or less distinct clinical courses of the disease are observed. However, at the onset and during the active stage of the disease, the general clinical characteristics of the group of children who ultimately will recover are remarkably similar to those of the group who eventually will die of renal insufficiency.

HENRY L. BARNETT

Onset and active stage—Nephrosis begins most frequently with the insidious onset of edema, usually noted first about the eyes. Such minimal edema is often more apparent to the parents than to the physician. About one-half of these children are between one and three years old at the time of onset[b, 1-4] and the disease is somewhat more common in boys than in girls.[1] Characteristically the children and their families[c] have been very healthy before the onset of the disease.

From the time it is first observed, the edema

[a]It should be emphasized that the term *nephrosis* is used here to describe this condition in children irrespective of evidences of nephritis. In a recent review by the author and his associates,[1] the term *nephrotic syndrome* (rather than *nephrosis*) was used to designate precisely the same group of patients. Erroneous identification with other definitions makes neither term satisfactory. Thus, as used here, *nephrosis* may be confused with the term *pure or lipoid nephrosis* and similarly *nephrotic syndrome* may be confused with the *nephrotic stage of chronic glomerulonephritis*. Despite these inherent difficulties in terminology (again related to lack of knowledge concerning etiology) the term *nephrosis* appears to the authors to be the preferred designation at present.

[b]About two-thirds of the children are between one and five years old at the time of onset. However, the disease does begin in children over five years of age and occasionally in infants under a year. Present evidence suggests that the course of the disease and the final outcome are not consistently different in those children in whom the disease begins at these less frequent ages.

[c]At the onset of nephrosis in one child, the parents may ask about the possibility of a sibling developing the disease. We have always been very reassuring about this point and, until recently, have believed that the probability of the disease occurring in a sibling of a child with nephrosis was no greater than in the general population. However, among 105 children with nephrosis, we have observed 3 families, in each of which 2 children had nephrosis and recently in a series of 86 children observed in Zurich, Switzerland,[5] more than one child with nephrosis was observed in 7 families. In one of the latter families, there were 4 and in another 3 children with nephrosis. The disease has also been observed in twins. The true incidence of nephrosis in the United States (and there is no evidence that it is different here than in other countries) is not known and it is even difficult to make a valid estimate. Nevertheless, it is not reasonable to believe that the general incidence of the disease could account for the high familial incidence observed in these two series. On the other hand, the fact that no familial incidence was reported in a series of 208 children with nephrosis observed in Boston[4] and that, even if there is an increased probability of a sibling getting the disease, the chances still must be very low, should strongly contradict emphasizing this point to parents. With our present knowledge, therefore, we are continuing to reassure parents about the unlikelihood of siblings developing the disease.

may persist and progress either slowly or rapidly. More commonly, perhaps, the very slight periorbital edema subsides and reappears over a period of weeks. During this period the periorbital edema is often attributed to a "cold" despite the fact that nephrosis is preceded by frank infections in only about one-third of the children.[1,2] The edema may be misinterpreted also as an allergic swelling because of the frequency of allergy in the children or in their families.[5] Sooner or later, however, the edema becomes generalized and the true nature of the disease becomes apparent. The clinical course of the disease during the active stage following the onset is then characterized by edema of varying degree and duration. Some of the children remain edematous throughout the active stage whereas others have repeated exacerbations and remissions. The duration of the active stage is usually from one to three years although it may be as short as six weeks or as long as five or more years.

Examination of the urine and blood at any time during this period[d] will reveal the changes characteristic of nephrosis: proteinuria (1.0 to 15 or more gm. per day); low serum protein (4.0 ± 0.5 gm. per 100 ml.) and albumin (1.7 ± 0.4 gm.); and high serum cholesterol (730 ± 81 mg. per 100 ml.).[1] During this same period some of the children (the true percentage is not known) will have no other recognizable clinical or laboratory abnormalities; whereas others will have one or more of the following so-called evidences of nephritis: hematuria (2,000,000 to 9,000,000 red blood cells per 12 hour night specimen); elevated blood urea nitrogen (reduced clearance of urea); and hypertension.

According to our present view, all of these children have nephrosis and the most that can be said about prognosis during this period is that, although about one-half of such children will recover, the final outcome in an individual child cannot be predicted. It may be (although it is not established) that the recovery rate in a large group of children showing no signs of nephritis at the onset is higher than that in the group showing such signs. However, the presence or absence of signs of nephritis at the onset does not permit prediction of outcome in an individual child, since during the course of the disease the same child may at one time show and at another time not show such signs.

Final outcome—However the disease may have begun, and in the absence of serious complications, the clinical course of nephrosis in an individual child tends to follow one of three general patterns characterized in terms of final outcome by: (1) active clinical disease followed by partial or complete remission; (2) active clinical disease with death during the active stage; (3) active clinical disease followed by chronic renal disease. It is difficult even to estimate the proportion of children with nephrosis who might be expected to follow each type of course.[e] The estimates given here are derived from an analysis of the course of the disease in all of the children with nephrosis treated at The New York Hospital-Cornell Medical Center between July 1, 1946 and June 30, 1953. Of the 105 children with nephrosis seen during this seven year period, the present status of 87 is known. Of these 87 children, 27 (31 per cent) are still in the active stage of the disease and therefore cannot be considered in estimating the final outcome of the group. The duration of the disease in these children in the active stage has been from three months to

[d]Occasionally, a child who has never had any recognizable edema is found to have unmistakable laboratory evidence of nephrosis (proteinuria, hypoalbuminemia, hyperlipemia) with or without evidences of nephritis. In our experience, edema has ultimately appeared in these children, although in some instances not for many months. Since, in rare instances, the total duration of nephrosis may be as short as several months in children who do show edema at the onset, it seems conceivable that a child could go throughout the course of the disease without edema and without the disease being recognized.

[e]The chief difficulty in making such an estimate is the uncertainty of final outcome in the living children. The high incidence of deaths from infections prior to 1937 together with the relatively small number of children seen in any one clinic (a project to analyze results cooperatively in many large clinics is in progress) has limited the necessary long-term follow-up observations on the outcome of the kidney disease, per se, in a large group of children with nephrosis. Until reliable data are available, therefore, any estimate of the over-all prognosis in nephrosis must be considered as very tentative.

as long as three and a half years.

The present status of the remaining 60 children is as follows:

(1) Children with active disease followed by partial or complete remission: Of the 60 children, 33 (55 per cent) are in partial or complete remission. The median age at the time of onset of the disease in this group of 33 children was 2.6 years (mean age 3.1 ± 1.6). In 11 of these children there was evidence of nephritis (hematuria, hypertension or reduced kidney function) at the time of the first examination.

All of these 33 children have been free of any symptoms of nephrosis for over a year; they all have normal renal clearances and normal values for serum total protein, albumin and cholesterol and no hematuria (less than 1,000,000 red blood cells per 12 hour night specimen). Of these 33 children, 17 (28 per cent of the total 60 children) have no proteinuria (less than 80 mg. of protein per 12 hour night specimen); the remaining 16 (27 per cent of the total 60 children) do have persistent proteinuria.

Since we are including in this group children with persistent proteinuria, it has to be anticipated that there may be recurrences in some of them. Consequently, although the prognosis for all of the children in this group is considered to be good, it is not implied that they represent a group of children who have recovered or who will recover completely. There are several reasons for us not to attempt at this time to identify within this group those children whose recovery will be complete and permanent. Thus, although it was believed previously that once proteinuria disappeared recovery was assured, recent experience has indicated that there may be recurrences several months after the urine becomes normal. We believe therefore that, although the prognosis is excellent for any one of these children who has no proteinuria, a longer period of observation is required before any group of them can be considered to be completely and permanently recovered.[6]

(2) Children dying during the active stage of the disease: Of the 60 children, 18 (30 per cent) died during the active stage of the disease at periods ranging from 10 months to 3.5 years after the onset. In 16 of these 18 children (27 per cent of the total 60 children) the major cause of death was renal insufficiency. Of the other 2 children, 1 died from an overwhelming infection due to *Pseudomonas pyocyaneus* and the other with marked electrolyte imbalance probably due to too severe salt restriction. Excluding these 2 children and 1 other child who was 13.3 years at the onset of the disease, the median age of the 15 remaining children in this group was 2.8 years (mean age 3.0 ± 1.9) which is remarkably similar to that of the group of children in remission. In 11 of these children there was evidence of nephritis at the time of the first examination.

(3) Children with active disease followed by chronic renal disease: In 9 (15 per cent) of the 60 children the active stage of nephrosis has been followed by chronic renal disease. Six of these children have been relatively asymptomatic for from one to five years after the active stage but they all have persistently reduced kidney function. Three of these 9 children (5 per cent of the total 60 children) have died of slowly progressing renal insufficiency after equally prolonged asymptomatic periods. In the present state of our knowledge, it must be anticipated that the remaining 6 children in this group will die of renal insufficiency, although when this might occur cannot be predicted.

Treatment

It must be questioned at present whether or not the course of the kidney disease in children with nephrosis is influenced by any available method of treatment. Although it thus must be accepted that neither prophylaxis nor specific treatment is possible, proper treatment still is of paramount importance. The physician caring for a child with nephrosis must make many decisions of great importance not only to the child but also to the family. Although some of these decisions are based on evidence which the physician knows is tenuous, nevertheless, they must be made and the parents must accept them even when they conflict with advice given by others. In

our experience, such acceptance, as well as acceptance of the disease itself, is achieved best by full explanation to the parents of as many facts about the disease as they are able to understand.[7] The following suggestions concerning treatment of a child with nephrosis represent those which appear to us to be most reasonable at the present time.

Diet—With the exception of moderate restriction of salt, a child with nephrosis should be offered a diet that is considered optimal for a healthy child of his age and the usual psychologic principles concerning feeding should apply. We recommend restricting salt only to the extent that foods are not cooked with salt, it is not added at the table, and very salty foods like bacon and pretzels are avoided. On the principle that too rigid salt restriction may lead to salt depletion, we do not advise low salt milk or bread preparations.

The major deviations of these recommendations from those previously (and still widely) advocated are that a high protein diet is neither urged nor even offered and, as in a well child, variations in the child's appetite are respected.

Activity—No restrictions are placed on the activity of a child with nephrosis beyond those which he, himself, may impose during periods of massive edema.

Contact with other children—Parents are urged to let the child with nephrosis play with other children, but because exacerbations of edema may follow common respiratory infections, as discussed subsequently, some limitations are imposed. Thus, when visiting another child more than the usual amount of attention is paid to whether or not the child has an infection and contact with large groups of children is avoided. To minimize the effect of these limitations, at present we are attempting to provide a modified nursery school experience for some of our children with nephrosis by arranging supervised group activity for two to four children living in the same neighborhood.

Hospitalization—A child with nephrosis should be at home as much of the time as possible. If parents realize that the physician is aware of the psychologic undesirability of hospitalization, they will accept more readily his decision that, at certain times, hospitalization is necessary. The major reasons for admitting a child with nephrosis to the hospital are severe infections, special treatment and evaluation of status.

Infections—The prevention and treatment of infections in a child with nephrosis constitute two of the major facets of treatment. In such a child, infections are important from two rather distinct points of view.[4] During remissions, mild respiratory infections (colds) may be accompanied or followed by exacerbations of edema. Secondly, during exacerbations, the child with nephrosis is very susceptible to severe generalized infections. Peritonitis, which may be accompanied by septicemia and cellulitis, is the most common of these severe infections. The presence of ascites may mask the classic signs and symptoms of peritonitis and it must be suspected, therefore, whenever a child with nephrosis develops a fever and looks sick. The fact that these infections were the cause of death in over 50 per cent of children with nephrosis before effective antimicrobial drugs were available emphasizes the importance of early diagnosis and vigorous treatment. Whereas in the past the pneumococcus caused most of these infections, at present they are due more frequently to other organisms and probably most often to *Escherichia coli.* An attempt should be made to determine the organism from blood and ascitic fluid cultures[†] but treatment should be started promptly with large doses of antimicrobial therapy designed to provide the broadest possible coverage.

The value of giving continuous prophylactic antibiotics to children with nephrosis is not yet established. It seems unlikely that the mild respiratory infections leading to exacerbations of edema would be prevented by such treatment, which might, however, decrease the incidence of the severe generalized infections.

[†]The question frequently arises as to whether or not an abdominal paracentesis should be done in the presence of peritonitis and particularly when there is accompanying cellulitis of the abdominal wall. Since unusual organisms which require specific antimicrobial treatment are occasionally encountered, it is our present opinion that a diagnostic paracentesis should be done.

Observations are in progress in the attempt to assess the value of giving prophylactic antibiotics. In our own clinic one-half of the children are receiving oral penicillin[g] (300,000 units of a liquid preparation once a day or 200,000 unit tablets twice a day) alternating at four week intervals with oral TERRAMYCIN®[g] (5 mg. per kilogram twice a day). The other one-half of the children are receiving the same drugs, again prophylactically against the severe infections, but only when they actually have a mild respiratory or other infection or when they are intimately exposed to an infection in another member of the family. We are not able, at present, to evaluate the relative effect of these two particular regimens on the incidence of infections in the two groups. However, we do recommend liberal use of antibiotics in children with nephrosis.

Treatment of edema, per se—Of the many agents or procedures which have been suggested for relieving edema in children with nephrosis, the only one we use specifically for this purpose at present is abdominal paracentesis.[h] The only other agent that we believe may be of practical value in relieving edema is dextran and we do not believe its value is established as yet. Among the agents or procedures which are used elsewhere and which we specifically do not use are osmotic diuretics (e.g., urea), mercurial diuretics, very low salt diets, and thyroid extract.

Specific treatment—It has been established that a number of agents (corticotropin or cortisone,[8-12] nitrogen mustards,[13,14] thiosemicarbazone,[5] measles virus[15]) are capable of inducing in edematous children with nephrosis the same type of profuse, sustained diuresis which occurs spontaneously or occasionally following severe generalized infections. In adequate dosages, either corticotropin (25 mg. intramuscularly every six hours for 10 days)[i] or cortisone (50 mg. by mouth every six hours for 10 days)[i] induce diuresis in 60 to 80 per cent of the trials and appear to be the agents of choice at the present time.[j] If cortisone is as effective as corticotropin in inducing diureses, it would be *the* agent of choice since it can be given by mouth.[12,16] At present, we do not believe a clear choice can be made between the two hormones and we use either one or the other.

There are many pertinent questions concerning the use of either of these hormones to induce diureses in children with nephrosis:

Should corticotropin or cortisone be given?—As stated earlier, if we were certain that the only effect of the hormones was to relieve edema, it is our present opinion that, because of known and perhaps additional unknown dangers inherent in their use, they probably should not be used. On the other hand, it has been demonstrated that, in addition to inducing diureses in children with nephrosis, these hormones have fairly reproducible effects on many of the known physiologic and biochemical characteristics of the disease.[17-25] These effects are in the direction of improvement (decreases in proteinuria,[17] hyperlipemia,[18,19] sodium-retaining substance in urine,[20,21] antidiuretic hormone in blood,[1,22] excessive potassium excretion;[23] increases in serum albumin,[17] glomerular filtration rate,[20] renal blood flow[24]) and suggest that the hormones favorably influence the basic disease process. It is for this reason that, at present, we believe corticotropin or cortisone should be given to induce diureses in children with nephrosis.

When should corticotropin or cortisone be given?—We have been recommending that hormone treatment should be postponed for

[g]The two drugs being used are BICILLIN® generously supplied by Wyeth, Inc. and TERRAMYCIN® Oral Suspension and Oral Drops generously supplied by Chas. Pfizer & Co., Inc.

[h]We are not including corticotropin and cortisone in this category because if we knew that these hormones did nothing more than relieve edema we would probably not recommend them.

[i]These daily and total dosages of the hormones are empiric but are those generally used to induce diureses irrespective of the age or size of the child. More refined dosage schedules have also been suggested[11] (e.g., corticotropin: 150 to 200 mg. per square meter per 24 hours, intramuscularly; cortisone: 300 to 400 mg. per square meter per 24 hours, by mouth. Both are given in four equally divided doses at six hour intervals).

[j]Some observers believe that remissions following diureses induced by measles are more prolonged or complete than those induced by other agents. We do not believe that present evidence supports this opinion.

six to eight weeks after the onset of the disease or of an exacerbation in the knowledge that about one-half of the children will have diuresis without hormone treatment within the first two months of the disease.[k] However, if future evidence should indicate more clearly that the hormones do affect the basic disease process, it would appear more reasonable to give them as early as possible in the course of the disease.

Contraindications to corticotropin or cortisone—Treatment with hormones should not be started in the presence of active infection. Reduced kidney function in an edematous child with nephrosis in the active stage of the disease should not preclude treatment with the hormones. Since the induction of a diuresis may be associated with improvement of kidney function, the presence of reduced function may increase rather than decrease the indication for treatment. On the other hand, hormones should not be given to those children who have progressed to the stage of chronic renal insufficiency.

Measures to prevent complications of hormone treatment—Because the hormones may mask evidences of infection in these children who are so susceptible to infections, it is important that therapeutic doses of antimicrobial therapy designed to provide the broadest possible coverage be given during treatment with the hormones. Sodium restriction should not be too rigid and adequate potassium should be given. During treatment with the hormones we give the diet recommended in an earlier section of this paper and add to it about 3 mEq. (0.22 gm.) of potassium chloride per kilogram of body weight. Some elevation of the blood pressure occurs in many children during treatment. The development of marked (above 140-150/100-110 mm. Hg.) and sustained hypertension requires that the treatment with hormones be withheld or stopped.

Corticotropin or cortisone after diuresis—Most of the experience during the past four to five years has been with short courses of hormones given to induce diuresis. Subsequent treatment has been given in the form of additional short courses only if edema recurred. However, because of the possibility already discussed that treatment with the hormones might have a favorable effect on the basic disease, recently more prolonged treatment has been tried. Thus, after a diuresis has been induced by the hormones, prolonged treatment with either corticotropin or cortisone has been given using various regimens, of which the following are representative: (1) giving corticotropin or cortisone for three consecutive days each week for several weeks;[26] (2) retreating with a full short course beginning when the child is free of edema five or six days after the end of the initial course;[27] (3) continuing the hormones after diuresis in full or reduced dosages for periods of weeks or months.[28,29]

It is not known at present whether or not the hormonal treatment of children with nephrosis, either for short periods to induce diuresis or for longer periods, has favorable effects on the final outcome of the disease.[1,11,12,30,31] Until this knowledge is available from careful clinical observation of large numbers of children over long periods of time, we cannot be certain that the hormones should be used at all. As stated earlier, the favorable biochemical and physiologic effects associated with diuresis induced by short courses of the hormones lead us to believe that such short courses should be given. However, in regard to prolonged treatment, it is our present view that until there is more certainty concerning its value, the risks involved are such that it should not be generally recommended.

[k]One or more courses of the hormones were given to 15 of the 33 children in remission and to 9 of the 16 children who died of renal disease in the active stage. Most of the remaining children were not treated because they had been through the active stage before we had begun using the hormones. However, in 5 of the children who are now in remission, no treatment was given because diureses occurred without treatment within the first two months of the disease.

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NEW BOOKS RECEIVED

New books received are acknowledged each month. As space permits, books of principal interest to our readers will be reviewed more extensively. Reviews and additional listings will be found in this issue starting on page A-104.

Pregnancy Wastage: Proceedings of a conference sponsored by the Committee on Human Reproduction, National Research Council in behalf of the National Committee on Maternal Health, Inc. Edited by Earl T. Engle. 254 pages with 82 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $8.50.

Antiseptics, Disinfectants, Fungicides, and Chemical and Physical Sterilization. Edited by George F. Reddish, Ph.D., St. Louis College of Pharmacy and Allied Sciences, St. Louis. 841 pages with 71 illustrations and 130 tables. 1954, Lea & Febiger, Philadelphia. $15.00.

1954 Medical Progress: A Review of Medical Advances During 1953. Edited by Morris Fishbein, M.D., Clinical Assistant Professor of Medicine, University of Illinois College of Medicine, Chicago. 345 pages. 1954, The Blakiston Company, Inc., New York and Toronto. $5.00.

Salmonellae and Shigellae; Laboratory Diagnosis Correlated with Clinical Manifestations and Epidemiology. By Alfred J. Weil, M.D., Department of Bacteriology, The Bronx Hospital, New York and Ivan Saphra, M.D., Department of Bacteriology, The Beth Israel Hospital, New York. 247 pages with 29 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $7.75.

Physiological Methods in Clinical Practice. By William S. Middleton, M.D., Department of Medicine, University of Wisconsin Medical School, Madison. 40 pages. 1953, Charles C Thomas, Springfield, Illinois. $1.00.

Nash's Surgical Physiology. Revised and edited by Brian Blades, M.D., Professor of Surgery, The George Washington University School of Medicine, Washington, D.C. Ed. 2. 686 pages, illustrated. Charles C Thomas, Springfield, Illinois. $12.50.

The Size and Growth of Tissue Cells. By Joseph G. Hoffman, Ph.D., Director of Cancer Research, Roswell Park Memorial Institute, New Mexico. 102 pages with 13 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $4.00.

GENERAL PRACTICE *Review*

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

Depressive Illness

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HERVEY M. CLECKLEY

DEPRESSIVE illness is a common psychiatric disorder that concerns all who practice medicine. It occurs in degrees of severity that range from a change of mood scarcely recognizable as illness to psychosis so gross and so typical that no one could mistake its nature or its seriousness. Mild or moderate depressive disorder may exist masked under widely varying physical complaints which prompt the patient or his family to consult the surgeon, the internist, the general practitioner or, perhaps, the otolaryngologist. Unlike many psychiatric conditions this is one which often endangers the patient's life. Even in apparently mild depression, the possibility of suicide should never be ignored. It is likely to be a grave and prolonged disorder if allowed to run its course. But in sharp contrast to the prospect 20 years ago, prompt relief usually can be obtained by treatment.

It is my impression that physicians in other branches of medicine are more likely to misevaluate depression than any other psychiatric disorder. This is readily understandable when one remembers that most physicians practicing today studied textbooks that emphasized manic-depressive psychosis and involutional melancholia almost to the exclusion of the types and stages of affective disorder the general practitioner is most likely to find in his office. I believe that even our most modern texts, though they mention "neurotic" or reactive depressions, fail to deal adequately with the most common picture of affective disorder.

The physician who thinks chiefly in terms

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of manic-depressive psychosis may first be overinfluenced by the term *psychosis*. Although he realizes that such depressions often begin mildly and progress gradually, he may find it difficult to reconcile the traditional concept of a delusional major disorder with his patient, who even after months of illness remains distinctly rational.

Most of the depressed patients I have seen and treated over the past 16 years in the psychiatric section of a general hospital did not appear to be cases of manic-depressive psychosis, depressed type (or involutional melancholia) or reactive depression. Those who have had previous or subsequent manic attacks and those whose depression occurred in what is commonly regarded as the involutional period, or in response to some objective event such as the loss of a loved one or some major reversal of fortune, all combined would scarcely equal the number who lacked these features.

Recognition

How are such patients to be recognized? It is not difficult with most of them. Typically the complaint is literal: Sadness, despondency and inability to hope. Usually such a patient lacks energy, saying that even the smallest task taxes his powers. Often he shows a specific inability to make decisions. Many persons suffering from this illness do not emphasize their sadness or dejection in the early stages. The chief problems may be stated as inability to sleep, loss of appetite, an unaccountable disinterest in work, dislike of meeting people, a deep sense of inertia, and lack of former confidence in themselves. Ordinary work has become an intolerable burden. Games or sports which they once followed enthusiastically now seem pointless. Some of them will say that nothing seems to matter anymore and, others, that they can't think clearly. A formerly high-spirited woman may complain that she has lost all incentive, that nothing seems worth doing. Some will say they are "run-down," that food has no taste, that everything irritates them, that they cannot find satisfaction or tranquillity for even a moment. Often, it appears as though the feeling or color had been bleached out of daily experience, leaving existence a dry formality without essence or meaning. Thinking that some physical illness is causing their trouble, they may go to the family physician and call for extensive physical examinations. When asked specifically if he ever feels like shedding tears, such a patient may weep for the first time during the interview.

In contrast with many psychoneurotic patients who seem to be exaggerating their symptoms, depressive patients give no such impression. On the contrary, it is typical of them to hold back or to minimize what distresses them most. The worry of a somatized patient about nonexistent heart, stomach or gallbladder pathology may contain genuine anxiety, but sometimes he also appears to take a positive satisfaction, a kind of wry pleasure, in recounting his infirmities. The distress of a depressed patient, whether he is entirely rational and has no explanation for his dejection or is psychotic and condemns himself for imaginary crimes, is solid and unmixed. With the exception of very agitated persons in whom anxiety mingles with the depression, these depressive patients tend toward understatement and react stoically to what is truly dreadful.

Sometimes the typical despair is not prominent or explicit. Instead of describing an anguish in positive terms, some patients complain chiefly of an inability to experience their habitual sentiments and fundamental motives. The devoted wife and mother reports that she no longer can feel any love for the husband she has passionately adored and no affection or even interest in her children. The patient does not turn against his loved ones. Instead, he is so deprived of basic feeling that what was formerly spontaneous, warm and real now has no subjective substance. Let us compare the "structure" of personal relations to an intricate system of pipes and sprinklers that irrigate a garden or to the wiring that conveys current to illuminate a city and activate its factories. If the key valve is closed at the source of water, nothing flows through the pipes that have kept our gardens fresh and luxuriant. If a master switch is broken at the dynamo, no current comes through the wires

that once brought light, warmth and vigorous energy to our city. Like the pipes and the wires in these too simple analogies, the attitudes and intentions of the patient are unchanged and undamaged. The current, however, has been cut off involuntarily and inexplicably; no feeling flows.

Most patients experience not only misery and despair in varying degrees but also self-condemnation. If there are no delusions to account for the guilt felt by a patient, often he will re-evaluate the ordinary conduct of daily life, or even deeds of remarkable virtue, to justify damnation on himself. An intelligent and attractive young wife treated recently longed to die and insisted that it was even beyond God's capacity to forgive or to spare her the eternal torment she claimed she deserved. Unable to recall any serious misdeed and incapable of delusion in the usual sense, she reinterpreted many distinctly magnanimous acts—faithful warm-hearted devotion to her husband and children, years of sincere work in church and Sunday school—as the essence of iniquity. Looking back through the horror of her present affect, she saw herself as having neither felt nor willed inwardly as she should have in any of the admirable behavior that constituted her past. She denounced as the empty mockery of a hypocrite the deeds that an intact reason prevented her from designating objectively as evil. After recovering from her illness, this genuinely good person, despite a becoming modesty, had no difficulty in distinguishing her real motives from those of a hypocrite.

Sometimes the misevaluation of actual events becomes so extreme that perhaps it deserves the rank of delusion. Another depressed patient did not attribute her remorse to imaginary acts but to the indisputable fact that, throughout her life, she had breathed air and drunk water. In suicidal despair, she felt with a terrible intensity and depth of conviction that this use of the earth's supply of oxygen and water had diminished that necessary to sustain the lives of others and constituted a crime deserving capital punishment and eternal isolation from the mercy of God.

In psychotic cases, not distorted by paranoid or schizoid features, the delusions invariably support the patient's conviction of hopelessness, his sense of guilt, his suffering and self-condemnation. A wealthy patient seen recently falsely believed himself bankrupt and insisted he could not be taken to a physician because his car—a new and perfect Buick—had no pistons in the cylinders and had not even wheels on which to roll. Another insisted that her viscera had putrefied from the effects of foul disease acquired in sin and that her veins and arteries contained no blood, only a mephitic pus that carried stench, moral corruption and malignant infection to everybody within miles of her. Still another woman sat for hours locked in the anguish of remorse over nonexistent adulteries. These, she was convinced, had taken place on a train when, several weeks before the onset of illness, she had made an overnight journey. Although the train carried approximately a dozen Pullman cars and well over a hundred men, she was certain that all of them, including the engineer, the conductor and the porters, had participated with her in the boisterous and implausibly energetic night of iniquity pictured in her delusion.

It is unlikely that any physician would have difficulty in recognizing severe or advanced depression. If despondency is still mild, hope still entertained or sought by the patient and delusions absent, some physicians, although aware that the disorder is affective, may underestimate its seriousness. The complete absence of all criteria by which a psychosis is defined, of all manifestations ordinarily associated with a major psychiatric disorder, may tempt the inexperienced practitioner to conclude that he is dealing with a trivial condition that is likely to respond to simple psychotherapeutic measures. Although some depressive reactions do subside quickly, and sometimes with no treatment at all, it is necessary to realize that many such conditions become progressively worse month after month and that every hour of illness is an hour of authentic woe. It cannot be emphasized too strongly that neither the absence of delusions nor an apparently mild or moderate degree of despondency can be taken as assurance that

the patient will not attempt suicide and perhaps achieve it, even though he may deny such inclinations.

I see no valid reason for the official term "psychoneurotic depression." Some physicians may feel that such a designation is appropriate for an emotional illness in which gross disorder of reasoning and other traditional criteria for establishing psychosis are not demonstrable at the time of examination. To most physicians, however, such terms as "psychoneurosis" and "neurosis" are likely to imply a mild disorder and perhaps to mislead to the dangerous illusion that the patient (since he is "only neurotic") can be relied on not to harm himself. Dear to some psychopathologists is the belief that a different etiology or "dynamics" distinguishes the nondelusional depressions from others. Although familiar for two decades with these theoretical formulations, I have found them neither clinically applicable nor of practical value.

Chamberlain[1] has called attention to a group of patients whose depressive manifestations are obscured, or even completely masked, by somatic complaints and other symptoms that usually indicate psychoneurosis. Although many of these patients come to the physician primarily to obtain relief from headache, digestive disturbance, dysmenorrhea or abnormal fatigue, persistent examination usually will elicit pathologic despondency. Sometimes the patient deliberately withholds or minimizes his depression, even when it is the chief source of his distress. In an early depression, the fear of appearing "neurotic" or cowardly, the fear of being suspected of "mental trouble" or a hope that the somatic symptoms indicate some physical illness that is the cause of his emotional state often seems to play a part in this evasion. It is common for depressed patients, whether or not the affective disorder is masked, to have a deep conviction that their loss of joy and hope, their inordinate self-reproach, are part of a personal or religious problem outside the province of medicine. The belief that no physician can help in such a matter may influence some patients to present chiefly, or only, a façade of physical complaints.

Therapy

Few developments in medicine during the last 20 years have afforded such adequate relief for such distressing disabilities as has the application of electric convulsive treatment to depressive illness. Although considerable differences of opinion persist about the value of this treatment in schizophrenia and other psychiatric disorders, it is difficult to see how anyone who has personally dealt with depressed patients before and after this method became available can question its efficacy. Its influence on depressive disorder of all degrees can, I think, be compared fairly with the influence of penicillin on lobar pneumonia. Prior means of treatment have not impressed me as more specific or more satisfactory than measures used in pneumonia before the earliest serum was available. Early and crude technics of convulsive therapy, although entailing little risk to life, often caused minor skeletal injuries and occasionally serious ones. The appearance of a patient undergoing a major seizure, his contorted face, his violent clonic movements and his dyspneic resumption of respiration dramatically suggest lay concepts of a death struggle. No doubt this contributed to the popular lay opinion that such therapy is too drastic to be considered, except perhaps as a slightly preferable alternative to permanent and total psychosis. Patients treated by early methods occasionally awoke in considerable anxiety. Many developed a profound dread of the procedure. Public knowledge that "shock treatment" was used in state hospitals for "the insane" promoted a feeling among some patients and their relatives that it was not only an extremely drastic measure but one which branded all who took it with the stigma of "lunacy," and "brought disgrace on the family."

Subsequent developments in the technic of electric therapy have so modified the patient's motor response that the risk of serious complication is now extremely small.[2,3] Virtually all possibility of fracture can be eliminated by the preliminary administration of succinyl choline.[4] Patients undergoing treatment by present methods seldom develop anxiety on

awakening. For the few who do, the anxiety can be substantially relieved by the preliminary administration of barbiturates.

The temporary forgetfulness and confusion regularly caused by early methods can be reduced by the proper use of modern instruments to a point where many patients with serious depression can receive adequate treatment without appreciable inconvenience from this complication.[2,3]

Patients in whom affective disorder is recurrent are not relieved of their tendency to develop depression again in the future by an ordinary series of treatments. Fortunately, as Stevenson[5,6] discovered some years ago, recurrence usually can be prevented by an occasional treatment given prophylactically at monthly intervals. When the patient's history shows a persistent recurrence of depressive attacks with relatively short periods of intervening health, this method of prophylaxis is often advisable. Memory is so slightly and so briefly disturbed by a single treatment with currently available technics that most patients need not put aside their regular work on the day it is given.

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Physical Diagnosis in Modern Medicine

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The place of physical diagnosis will occupy a greater field in the future than it did in the past. The significance of the history and the physical findings, having been established through the laboratory, furnishes evidence of specific types of infections and biochemical states. The clinical syndromes of such conditions are so definite that their etiology is apparent. At least, by critical evaluation of the signs and the symptoms, the clinician is not dumbfounded if laboratory facilities are not available.

In a short span of years, the statement of an eminent physician that he "practically never" needed the use of an x-ray examination, has become inconceivable. Now the reverse problem presents itself; the patient is first run "through the mill" of laboratory procedures before a serious diagnosis is attempted.

Because of the multiplicity of informatory laboratory procedures now available, the place of physical diagnosis has become more important than ever. It shows what "diagnostic paths to tread."[1] It indicates what laboratory procedures to choose. If these measures are

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not chosen as indicated by the history and physical findings, the result will be chaos and confusion.

Too often, the seasoned practitioner sees the errors due to wrong emphasis on some details. What Cardozo[2] said about law is equally true in medicine: "There is an accuracy that defeats itself by overemphasis of details." Wrong emphasis frequently is a stumbling block in diagnosis. Examples are numerous, such as the blind acceptance of a basal metabolic rate of plus 46 when the patient complained of an intolerance for cold and was very happy in the summer heat. This was very obviously a technical error.

Unfortunately, medical students and interns are no longer experienced in technical procedures and are willing to accept results of any novice to whom many procedures are relegated. One soon loses confidence in the accuracy of the laboratory when even blood counts show a variation of 30 per cent from day to day or from one laboratory to another. This is further explained when one sees a technician "milk a finger" for blood or fail to cleanse the end of a pipet which carries a significant amount of blood. The history and physical examination not only must direct, but also must evaluate all of these informatory procedures.

A detailed medical history is the most important step to making a diagnosis. To know the history, the examiner, himself, had better take the information. If not, it will be necessary for him to review it, which frequently proves more time-consuming and less satisfactory.

A medical history is a record of the symptoms experienced by an individual as result of a disease process, an abnormal function of organs or an injury. The condition causing these sensations may be apparent to the senses of sight, touch, hearing, smell, or even taste. These comprise objective evidence and are called signs. A medical history is concerned only with symptoms.

In a sense, a medical history is a theme and is governed by the rhetorical principles of a theme. The medical historian can well revert to his training in English in high school or in college. He can properly be governed in writing a good medical history by the same principles: (1) unity, (2) coherence, (3) clarity, (4) conciseness, (5) logical sequence, (6) emphasis and proportion to proper events and (7) proper expression with good use of words. There may even be a beauty of expression, such as is manifested in the medical writings of Sir William Osler.

Exact quotations of the patients are at times the best way to record symptoms, but they are usually too verbose and frequently lack needed scientific vocabulary. To a certain extent, a medical history can be likened to a court procedure report: There is always a central theme which is maintained to elicit evidence on which to base a verdict or a diagnosis. Irrelevant details must be avoided.

Students frequently are advised to let the patients talk. This, however, can be permitted only to a very limited degree. It has also been said that if patients talk enough, they will talk themselves into a diagnosis. This rarely occurs; usually the patient talks himself out of a diagnosis, chiefly by confusing the examiner and by not keeping interrogation and conservation along channels which may offer information. Certainly, the immature student will become hopelessly confused by letting patients talk aimlessly. It requires tact, discretion, judgment and experience to shut off those who aimlessly wander, relating irrelevant details. Nevertheless, some patients must be encouraged to talk.

The patient must not be discouraged from talking by a preconceived notion of his examining physician. The physician must not direct his questions to justify a thought that he may have, but, in general, must ask very indirect questions. Answers to pertinent questions give ramifications to follow in getting a correct exposition of the patient's symptoms. Each question is determined by the answer to the previous question. It is only after all efforts have been exhausted by indirect questioning that direct questions are asked. For example, in questioning a patient with heart disease, an inquiry regarding his tolerance to certain daily activities may be very helpful. A good indirect question for the housewife would be:

"What happens when you climb stairs?" or, for a farmer: "How do you get along pitching hay?" You do not immediately ask him whether he is breathless after exertion.

No standardized, stereotyped record can record human sensations. The expression of such sensations varies from exaggeration by the extremely sensitive individual to suppression by the stoic. Practice and experience are necessary for differentiating and evaluating symptoms related by the patient. Good advice to students is: Begin early in your medical career to differentiate between nonessential and essential information.

The advice is often given that no notes of any sort are to be taken while questioning the patient for fear of restraining his expression. Mature experience justifies the conclusion that if one person is restrained, 10 are complimented and express themselves more fully. Furthermore, it is certain that few individuals have sufficient retentive power to memorize all the details which a patient may relate. It is an established fact that anyone taking a history should make temporary or permanent notes while the information is related by the patient. For making a record while the patient is talking, one should quickly develop the faculty for writing the answer to the last question while listening to the answer of the next question. This skill requires considerable experience but is immeasurably valuable when once accomplished.

The style of written history depends on the purpose for which it is taken. A medical student trying to perfect his technic in history-taking will probably not be able to complete a final product while listening to his patient. He will have to use sentence structure in order to convey impressions. When only one or two individuals read the histories, scanning styles may be adopted with only one or two words conveying the sense of a whole sentence. For this, we recommend reading the book, "Ulysses," not for content but for style. On the other hand, the present flare for using any abbreviations, which may enter any person's head and are not at all standardized, is to be absolutely discouraged. For example, S.O.B. has been associated for so many years with a definite meaning that it cannot be established to mean "shortness of breath." If abbreviations are to be accepted, some standardization must be made.

Obviously, the patient's name (and if a married woman, preferably her husband's surname with her first name) should be recorded. Age and occupation are important. But except for these details, there is no checklist history which is helpful. Checklist histories stifle the initiative, curb intelligent questioning and lead to mental sterility.

The systematic review of the development of present complaints will not be reiterated.

Social History

Social history is important in some cases, and if it seems important, it should be developed. It necessitates an exploration of life history since birth—experiences in school, in occupation and in marital life. It also necessitates the development of considerable subsidiary fields.

Psychosomatic and Psychiatric History

In taking general history, psychosomatic and psychiatric history may be approached as a single entry. At present, it seems logical that these problems should be approached in two different ways. One approach is for patients who simply are not able to adjust themselves to their own surroundings. Many of these individuals can be handled in quite common-sense ways, and, frequently, man-to-man conferences solve many of their perplexities. And another approach is for those who definitely belong in mental illness groups; their problems must be recognized, and they should be transferred to a qualified psychiatrist. It is not the scope of this history to enter this field.

It is becoming increasingly evident that many human emotional problems can be handled by a confidential talk between physician and patient without getting into the mires of psychiatry. However, if a deeper psychiatric approach is indicated, frequently, an amateurish approach to grave psychiatric problems is not helpful, but even harmful. Such a patient's information may be very interesting news, but it does not contribute to the pur-

pose of the history; namely, to establish a diagnosis.

Family History

If the history indicates that there may be a hereditary or a familial tendency, explore relevant facts thoroughly and intelligently. Do not spend or waste time attempting to get answers to the usual stereotyped questions about relatives, such as: "How old is your father? How is his health?" The family history must always be recorded at the end of the clinical history.

Physical Diagnosis Grading

It is not the purpose of this discussion to be so pedantic as to present the elements of physical diagnosis, but a few fundamentals will be rapidly rehearsed.

There is much confusion in grading physical signs and findings. The following system is presented for consideration. This grading is sufficiently accurate to convey an impression from one individual to another. It is doubtful if finer shades of grading can be used generally.

Grades of physical signs—Purpose: To indicate (1) presence, (2) intensity and (3) size.

Grade: (1) doubtfully present (further observation to establish), (2) slight intensity or small size, (3) moderate intensity or size, and (4) marked, intense, loud or large.

Risak[3] has critically analyzed fundamental procedures in "Der Klinische Blick" (The Clinical Glance). A translation of this small book serves a valuable purpose. The writer emphasizes: (1) means at the disposal of the diagnostician, viz., his sight, hearing, touch, smell and taste, (2) the gross evidence furnished by the patient and his surroundings, viz., temperament, position while walking, standing, sitting or lying, age, sex, size in stature or weight, skin or hair, veins or arteries, muscles and bones, hands and feet, and eyes and ears.

Evidence gained by these simple procedures frequently presents the physiognomy of disease. This was well expressed by Marshall and Hall.[4] "There is a physiognomy of disease as well as of individuals, and the simultaneous impressions of which it is constituted can no more be exactly represented by the successive enumeration of the symptoms and the signs than the countenance of a friend can be recalled by giving us a cast of each of his features in succession."

Among the specific physiognomies are included (1) the mitral facies with its malar hyperemia and deep crimson lips, (2) the broad, thick-lipped, impassive face of myxedema with the delicate rose-purple cheeks, (3) the lemon-yellow tint of pernicious anemia, (4) the anxious face, the moist warm skin of hyperthyroidism, (5) deficiency state, (6) dehydration and (7) types of dyspnea. The characteristic pictures of disease can be multiplied manyfold.

At present, the teaching of physical diagnosis is not guided by these principles. From another point of view, an attempt is made comparable to that of an artist, who instead of painting the whole picture, has "specialists" paint in succession the sky, the trees, the brook, the house and the animals, thereby hoping to produce a masterpiece. Teaching immature medical students by the contributions of specialists confuses him. He is unable to envision the picture as a whole.

Diagnosis consists of two distinct mental processes, an analysis and a synthesis.[5] Proper analysis is extremely important. It is guided by the facts derived from the history and the physical findings. The synthesis is a product of good insight and judgment, and it should improve with experience. Obviously, the usual methods of inspection, palpation, percussion and auscultation employed in physical diagnosis are not to be neglected. In pulmonary disease, restricted respiratory excursion and crepitant rales frequently precede densities demonstrable by roentgenograms by hours and even a day.

Graphic recording of sounds produced within the chest is evidence of a great contribution made from basic sciences to clinical methods, but the most optimistic vision cannot foresee its use at the bedside except as a means of clinical investigation.

It was an early hope that recording of heart sounds would clarify auscultation of the heart, as the electrocardiogram has done with ir-

regularities. At present, it has failed to do so.

Not all sources of error are found in the laboratory. The description of the apex beat has been grossly misrepresented, with only a rare exception, in all textbooks of physical diagnosis. Since the beginning of this science, the fact has been accepted that the apex can be located in practically all normal chests, whereas the critical palpation of the precordium can be located only in approximately 25 per cent of individuals of all sizes and ages.[5]

Another common error is evident when mathematical accuracy is attempted by measuring the distance of the left heart border from the midline in centimeters. Obviously, if very simple arithmetic is applied to these measurements, it becomes evident that the radius of a chest is greatly modified by the circumference of an adult chest measuring 32 inches and one measuring 48 inches. One can establish a much better estimate of the size of the heart by demonstrating the relationship to the midclavicular line. Since this is only an approximation, it could be expressed still more truly in finger breadths. In general, the tendency to convert approximations to mathematical accuracy is not justified and is uncritical.

Summary

In summary, the following facts persist: (1) History and physical examination are the beginning of all diagnoses. (2) Symptoms and physical findings have become more secure by x-ray findings and clinical laboratory procedures. By this correlation, the astute clinician can frequently predict or assume with assurance the laboratory finding without the findings or procedures or, at least, intelligently direct the procedures needed. (3) The master mind of medicine still remains the qualified and competent physical diagnostician.

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MEETINGS *and Postgraduate Courses*

Medical Library Association: Fifty-third annual meeting at the Hotel Statler in Washington, D.C., June 15-18, 1954. Armed Forces Medical Library will be the official host. Further information can be obtained from Lt. Col. Frank B. Rogers, Armed Forces Medical Library, 7th and Independence Avenue, S.W., Washington 25, D.C.

University of Minnesota, Minneapolis: Continuation course in radiology for general physicians, May 3-5, 1954, under the direction of Dr. Leo G. Rigler, Professor and Head, Department of Radiology. Registrants will spend most of their time in the University Hospital Department of Radiology reading films and carrying out procedures in association with members of the faculty of that department. Because of the nature of this course, registration will be strictly limited, therefore early application is suggested.

University of Minnesota, Minneapolis: Family Doctors' Days, May 5 under the direction of the Hospital Laboratories Department and June 9, the Pathology Department, at the University Hospitals. Further information may be obtained from the head of the department concerned or the Director, Department of Continuation Medical Education, 3330 Powell Hall, University of Minnesota.

University of Minnesota, Minneapolis: Continuation course in electrocardiography for general physicians at the Center for Continuation Study, May 10-15, 1954. Emphasis will be placed on practical experience in the interpretation of electrocardiograms. Separate sessions are being planned for those who consider themselves "beginners" in electrocardiography.

Editorials

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OPERATIVE DICTATION

WHY is it often difficult to obtain exact information from operative dictation?

This is a familiar question asked by interns, residents and any physician who, during a survey of hospital records, has found it necessary to examine operative dictation. There are times when hospital administrators, governing boards, record librarians, insurance adjustors and medicolegal experts are confronted with, and troubled by, this problem.

In the fictitious record of Mr. R. L. O., the two lines of operative dictation revealed that he had a "routine" appendectomy. What does this mean? It is known that his surgeon had done "routine" appendectomies and "routine" closures in an acceptable fashion for over 30 years. However, in this instance, a postoperative ileus accompanied by hiccoughs was complicated by dehiscence and secondary infection resulting in the development of a ventral hernia. Six months later the same surgeon repaired the ventral hernia by a "routine" layer-to-layer closure. In the past decade this surgeon had performed the majority of appendectomies in this hospital and "they say" he had changed his routine several times. He used to invert the appendical stump but recently he had simply tied it; he had abandoned the use of silk in favor of cotton for closures; he had "recently" started using wire for repairing ventral hernias.

In attempting to write a paper on colonic or rectal resections one may be unable to obtain the exact location of the lesion from the operative dictation. Partial exploration of the common duct is "partial" when it stops and starts where? What is a "modified" Bassini herniorrhaphy and in what manner is it modified? The subtotal gastric resection of Dr. X. is known to be different from that performed by Dr. Y. When Dr. Z. examined the records he found that Dr. X. removed the metastatic nodes part way to the celiac axis but he wonders how far is "part way"?

Confusion inexorably compounded in the name of brevity would inadequately characterize the operative dictation recorded in many hospitals today. The problem is real, it exists and it is capable of solution.

The solution to inaccurate, incomplete and even misleading operative dictation is the surgeon's responsibility. He should know and clearly define what vessels were ligated, what structures, organs or viscera were removed and, in some instances, the location of what was left intact, involved, uninvolved and not removed. We must not confuse accuracy with rigid conformity but we must return to more exact anatomic and pathologic descriptions of the range of our operative procedures. For many this will be merely a question of self-discipline but for some individuals it will be a problem of grammatical expression, of anatomic knowledge or even revised nomenclature. Whatever the individual problem may be it warrants personal study directed to improving the situation.

The hospital must provide adequate secretarial or mechanical facilities if this problem is to be solved. Surgeons may become justifiably delinquent if the irresponsible secretary is absent for 10 o'clock coffee. Have we not at some time or other cussed that infernal dictating machine and, on investigation, discovered that it was neglected, unrepaired and not in service—a mechanical orphan?

We could, of course, elaborate on the duty of the record librarian to recognize, but not interpret, incomplete operative dictation. We could place the record committee in the unenviable position of reporting delinquency and likewise place the administrator in the unhappy position of enforcing the rules and regulations, but is this desirable?

We may congratulate ourselves that surgery has progressed from the anatomic era through the pathologic era to the physiologic era. However we should not delude ourselves by thinking that a formidable array of milliequivalents will adequately describe the range of our operative procedures. There is no substitute for accurate and complete operative records. This is the surgeon's responsibility.

GARNET W. AULT

DEATH FROM DICUMAROL POISONING

THE Supreme Court of South Africa, in a decision rendered at Johannesburg on May 20, 1953, found a physician guilty of "culpable homicide" in causing the death of a patient for whom he had prescribed and administered DICUMAROL®. The court said that he had failed to exercise that "degree of skill, care, diligence and ability which he could reasonably be expected to exercise." Specifically he had failed, before administering and prescribing Dicumarol, to acquaint himself with the various strengths of dosages in which the preparation is purveyed or to specify on the prescription the strength or dosage to be dispensed; he had apparently been without any adequate knowledge of its effects and of its proper administration; he had failed to inform the deceased or her husband of the potentially toxic nature of the drug, of the precautions to be observed, and of the necessity of noting and reporting any signs of abnormal bleeding; he had failed to keep the deceased under observation or to arrange for her to be kept under observation; he had failed to use prothrombin index tests, and he had not taken proper and adequate measures when advised that the deceased showed signs of abnormal bleeding.

The jury brought in a unanimous verdict to the effect that he was guilty of the crime as charged and the judge imposed a fine of 75 pounds (roughly $200) or three months compulsory imprisonment.

The woman, who was married and 70 years old, had a femoral thrombosis. The doctor decided to treat the condition with Dicumarol and he wrote a prescription which read simply "Dicumarol, 40 tabs., one t.d.s. p.c." The pharmacist dispensed 40 tablets of 100 mg. strength each. The patient began immediately to take the tablets and continued for 13 days, taking in all 38 tablets or 3800 mg. of Dicumarol in 13 days. About a week after she began to take the drug, the patient's daughter noticed little black spots on her mother's legs, like blisters; three days later there was bleeding from the gums and from a

spot between the shoulders. When the doctor was advised by telephone of the patient's condition, he stopped the tablets but did not visit the patient or prescribe any treatment. From then on the condition, including the bleeding, became much worse with bleeding from the nose, the bladder and the mouth. Three days after the patient stopped the tablets the husband called the doctor who ordered vitamin K, 10 mm., but improvement did not occur. Then a local doctor was called and he arranged to move the patient to a hospital. Despite transfusions of fresh blood and injections of vitamin K, the patient died about 24 days after the Dicumarol was first taken.

The primary observation in the necropsy was multiple hemorrhages into the cerebellum and the fourth ventricle, the scalp, subarachnoid spaces, lungs, perivesical, retroperitoneal and perinephric areas. There was free blood in both kidney pelves, the ureters, the stomach and around the rectum.

The judge's definition of negligence in his summation to the jury was the usual typical statement that a physician is not required to bring the highest possible degree of professional skill but is bound to employ reasonable skill and care. In deciding what is reasonable, regard must be had of the general level of skill and diligence possessed and exercised by the members of the branch of the profession to which the physician belongs. This means that a physician in a skilled profession cannot shelter himself behind a defense that he did not know enough about it or was not sufficiently skilled.

Further, in summing up, the judge distinguished between specialists and general practitioners. When a general practitioner is tried, the test is not what a specialist would or would not do under the circumstances but what is the common knowledge in the branch of the profession to which the doctor belongs.

Interesting also was the court's statement of the precautions that should be taken in administering Dicumarol. Briefly, the court said that "The drug should not be administered unless prothrombin index tests have been taken not only initially before any dose is administered, but also daily while it is being administered, and, even when it is temporarily left off, in order to give the prothrombin level an opportunity of rising until the effect of the drug has been stabilised; and even after that there should be these prothrombin tests at intervals of two or three days. . . . Where there are no facilities for these tests to be carried out, then, of course, other precautionary measures must be followed. The next precaution is that while the drug is being administered the patient must be kept under observation and should be seen daily in the initial stages; perhaps not so frequently in the later stages when the effect of the drug has been stabilised."

The court also criticized the nature of the prescription written by the physician who retired behind the claim that he had not specified the strength of the tablets which the pharmacist supplied. To this the court said that the prescription was a faulty one. It was negligently made up in two respects: (1) The dosage to be given to the patient was not stated; (2) the tablets were mentioned without specifying their strength. The claim was also made that the pharmacist should have called the physician on the telephone in case the physician omitted to mention the dosage. The court felt that it "appears to be a very alarming suggestion, that a doctor who is supposed to have superior knowledge should be entitled, if he issues a faulty prescription, to shelter himself behind the chemist who makes it up." The doctor stated that he intended to prescribe 25 mg. tablets. The court asked, "Where could the accused have got this information about the 25 mg. tablets?" This seems to have been an afterthought of the physician when he was called to account. The court also made a considerable point of the physician's failure to visit his patient or to take other necessary steps when he was informed of the patient's serious condition and the bleeding. Actually he did not consult a medical book about the properties of the drug until after the patient was in an extreme condition and in the hands of the local physician.

The report[1] of this case in the *Journal of Forensic Medicine* is most informative and worthy of being read in detail by all who

are interested. It is supplemented by an excellent article on the pharmacologic and toxicologic aspects of Dicumarol by Professor F. Stephen-Lewis[2] of the Department of Pharmacology in the University of Witwaterstrand, Johannesburg. He points out that deaths associated with Dicumarol therapy are due to hypersensitivity, to lack of correlation with prothrombin or to toxic effects due to overdosage. In this case there was no evidence of hypersensitivity or of the prothrombin content of the blood. He stated that the fatal result may be attributed to cerebral hemorrhage from overdosage with Dicumarol. Finally, he notes that Dicumarol has been deleted from the 1953 British Pharmacopoeia and is replaced by ethyl-luscoumacetate (TROMEXAN®), a derivative of Dicumarol with the advantages of quicker onset of action and less tendency for cumulative effects, but requiring the same close supervision and prothrombin estimations, especially as sudden and unpredictable decrease in prothrombin levels may occur with this drug.*

What occurred in this case is instructive to every physician who administers any potent drug. Enough incidents have already occurred to indicate the necessity for extreme care and for the consultation of authentic reference material whenever potent drugs are prescribed, particularly when there is any doubt as to a drug's potential toxicity.

MORRIS FISHBEIN

1. Death from Dicoumarol poisoning: The Case of Regina vs. T. v d M. The indictment and the verdict. J. Forensic Med. 1:68 (October-December) 1953.

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*Dicoumarol, cyclocumarol and Tromexan are included in "New and Nonofficial Remedies." Dicumarol is accepted in 25 and 50 mg. tablets. The warning appears that prothrombin clotting times should be determined every day during therapy. If the prothrombin clotting time reaches between 30 to 35 seconds, dosage should be reduced to 50 to 100 mg. daily, and if it rises to 35, the drug should be withheld and not re-employed until the prothrombin time returns to 30 seconds or less. Under such circumstances the drug may be given cautiously in 100 mg. doses. An appearance of hemorrhagic manifestations indicates the administration of vitamin K by slow intravenous injection supplemented by transfusions of fresh whole blood.

POPULATION CHANGES

A RECENT summary* of changes in population in the United States from 1940 to 1950 emphasizes a few significant facts. Women are living longer than men, with a life expectancy at birth of 72.4 years for girls compared with 66.6 years for boys. This means that at age 60 there are three times as many widows as widowers. An increasing proportion of the nation's wealth and property is passing through inheritance into the hands of women.

The general trend of the population is westward and the West has almost tripled its share of the total population in the past 50 years, while regions east of the Rockies show slight declines. An average of over 3 per cent of the population moves to another state every year. Whereas two-fifths of the population lived in cities of 2500 inhabitants or over in 1900 and three-fifths lived in the country, the proportions have been reversed in 1950—three out of every five inhabitants are now city dwellers.

During the past decade, the migration of the Negro population has brought about a decline in the South and a rise in all other regions of the country. The number in the West almost tripled. The majority who move settle in cities. The foreign-born whites have declined in total population from 13.4 per cent in 1900 to 6.7 per cent in 1950.

Most recent statistics show that Americans are marrying younger. The excess of births over deaths rises. Our birth rate reached an all time low in 1933, began to rise in 1937 and reached its peak in 1947. Since that time there has been only a slight decline. These facts regarding population need to be borne in mind by all who are concerned with the economic, social and political needs of our people in the future.

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*Population Bulletin, Population Reference Bureau, Inc., Vol. 9, No. 8, December 1953.